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First-Incidence, Age of Onset Outcomes and Risk Factors of Onset of DSM-5 Oppositional Defiant Disorder from ages 3 to 9

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Running Head: INCIDENCE OF ODD

First-Incidence, Age of Onset Outcomes and Risk Factors of Onset of DSM-5

Oppositional Defiant Disorder from ages 3 to 9

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ABSTRACT

Objective To examine the one-year first-incidence and prevalence of oppositional defiant disorder (ODD), the outcomes on psychopathology and functioning by age of onset and the risk factors of onset of ODD from ages 3 to 9 in children from the Spanish general population.

Design Longitudinal with 7 follow-ups and double cohort (ODD and non-ODD children).

Setting General population of preschool and elementary school children in Barcelona (Spain).

Participants On a first phase the parent-rated Strengths and Difficulties Questionnaire conduct problems scale plus oppositional defiant disorder DSM-IV symptoms were used to screen for behavioral problems. The second phase sample size contained 622 cases at age 3 and at age 9 418 remained in the study.

Results The probability of the onset of ODD showed increasing values at ages 4 ($R =2.7\%$) and 5 years ($R=4.4\%$). These values decreased until age 7 ($R=1.9\%$) and increased again until age 9 ($R=3.6\%$). Up to 9 years old the cumulative risk of new cases of ODD was 21.9%. Early onset was associated with a higher risk of comorbidity and later onset with higher functional impairment. Subthreshold ODD, high scores in irritability and headstrong dimensions, ADHD and other comorbidity, negative affectivity until age 7, difficulties in inhibit and emotional control, punitive parenting and maternal internalizing problems were risk factors of a first episode of ODD during this seven-year period.

Conclusions The risk of new cases of ODD in the general population at preschool age and during childhood is high. Preventive interventions starting at preschool age are recommended. Given that the risk factors are consistently well identified in this and previous studies, targeted and indicated interventions should be implemented to lessen the developmental difficulties and school and family burdens that cause ODD.

Strengths and limitations of the study

- This is the first study that report on incident cases of oppositional defiant disorder from preschool to childhood.

- Strengths of the study are that the diagnostic information was obtained via semi-structured interviews based on DSM-5 criteria, the length of the follow-up period (7 years), the inclusion of two different developmental stages, preschool and childhood, and the fact that the values of incidence were not overestimated, given that previous diagnoses until age 3 were also made. Also age of onset through a prospective design. Furthermore, the information on risk factors was obtained from parents and teachers.

- The diagnostic information, based on data from just one source, the parents, and the lower participation of low SES families may have led to bias in the estimates. The internal consistency of some parenting scales make that parenting practices results should be interpreted with caution.

FIRST-INCIDENCE, AGE OF ONSET OUTCOMES AND RISK FACTORS OF

ONSET OF DSM-5 OPPOSITIONAL DEFIANT DISORDER FROM AGES 3 TO 9

According to epidemiological studies the proportion of children and adolescents with mental health problems is 13.4%(1). These disorders are stable and continue into later life with adverse adults outcomes(2). Therefore, childhood is a target period for the early identification and prevention of mental disorders.

Oppositional defiant disorder (ODD), a pattern of negativistic, defiant, disobedient and hostile behaviour, is one of the most prevalent disorders from preschool age to adulthood(3). The pooled prevalence is 3.6% up to age 18(1). ODD is accompanied by various concurrent disorders (attention deficit/hyperactivity disorder-ADHD), successive comorbidity (conduct disorder, anxiety, depression, substance use)(4) (5) and functional impairment(6). Symptomatology is stable and sufferers have difficulties in the transition to adulthood(7). The amount of children and families affected and the severe consequences that compromise healthy mental development underscore the need to know when the first onset occurs and the factors that predict this onset in order to plan appropriate preventive strategies.

Currently, we know how many children in the population are affected by ODD at a given point in time; that is, the prevalence, a measure of the status of the disease. We do not know, however, how many new cases appear at different developmental stages; that is, incidence, a measure of newly occurring cases of the disease during a specific developmental period(8). Because there is often a low number of incident cases, incidence studies require cohort designs with large size samples. Literature shows that there is a dearth of studies about the incidence of psychiatric disorders in childhood and adolescence. The available data on ODD mostly focus on adolescents and youths. Roberts(9) reported that the risk of new cases of ODD for adolescents in a 12-month period was 1.56% and Benjet(10) found a 5% 8-year

incidence for 19- to 26-year-old youth. There are no studies on the incidence of ODD during preschool and childhood. Neither do we know the differential consequences of the disorder according to age of onset. Literature on general mental disorders has reported that early onset is associated with greater severity, persistence and lack of response to treatment(11). Age of onset is an important data to advise on mental health policies(12).

Several risk factors have been reported in the literature on ODD. Child risk factors include genetic influences(13), difficult temperament(14), difficulties in processing social information(15), sex(16) and ADHD(17). The contextual factors reported include socioeconomic status, parenting practices, parental psychopathology, family conflict and poor attachment(13) (18). Incidence figures, which report on new cases of disease, are more useful for identifying risk factors than prevalence studies, which include both chronic and new cases(19). No previous studies have examined the risk factors of ODD by considering new cases. Only Roberts(9) adopted this approach in adolescents, reporting that a younger age, poor family satisfaction, passive coping and low mastery, school and economic stress and poor relations with parents were predictors of incident cases of ODD.

Furthermore, ODD is a continuous disorder that starts early in life and persists into adulthood(7). It is therefore imperative to know for prevention purposes how the early manifestations of ODD symptomatology affect the definite appearance of the full disorder. Several dimensions of ODD have been identified to explain its underlying structure: irritable (including loses temper, angry and touchy); headstrong (argues, defies, annoys, blames) and hurtful (spiteful-vindictive)(20). Rowe(18) showed how ODD dimensions predict full ODD diagnosis. Moreover, the literature has shown that subthreshold conditions are risk factors for developing similar (homotypic) or different (heterotypic) full-syndrome(21) and that they constitute a major public mental health burden(22).

The objective was to study annually the proportion of incident cases of ODD from ages 3 to 9 (preschool through childhood), to ascertain the differential outcomes by age of onset and to test if previously reported risk factors associated with ODD are prospective risk factors of incident cases at these developmental stages.

METHOD

Participants

The initial sample consisted of 2,283 children randomly selected from early childhood schools in Barcelona (Spain)(23). A two-phase design was employed. In the first-phase of sampling, 1,341 families (58.7%) agreed to participate (33.6% high socioeconomic status (SES), 43.1% middle and 23.3% low; 50.9% boys). To ensure that children with possible behavioral problems participated, the parent-rated Strengths and Difficulties Questionnaire (SDQ[3-4]) conduct problems scale(24) plus ODD DSM-IV symptoms were used to screen. Two groups were considered: screen-positive (all children with SDQ scores ≥4, percentile 90, or with a positive response to any of the eight DSM-IV ODD symptoms) and screen-negative (a random group comprising 28% of children who did not reach the positive threshold).

The final sample for the follow-ups (second-phase) included 622 children. The screen-positive group comprised 417 children (49.4% boys) and the screen-negative group 205 children (51.2%, boys). No differences in sex (χ^2 =0.07; p =.793) or type of school (χ^2 =0.72; p =.396) were found on comparing completers and drop-outs during the seven years of annual follow-ups. However, the SES of those leaving the study until age 9 was lower (χ^2 =20.89; p <.001).

From the initial 622 children, 65 who presented an ODD diagnosis at the start of the study (age 3) and 18 who left the study at the second follow-up (age 4) were excluded for the analysis of risk factors because lack of information (N =539). Decrements in sample size at

successive follow-ups were either due to attrition or to the exclusion of children who had

already presented a first ODD diagnosis. Demographic characteristics are shown in Table 1.

Measures

Diagnostic Interview of Children and Adolescents for Parents of Preschool Children (DICA-PPC)

The DICA-PPC(25) is a computerised semi-structured interview which generates diagnoses

through algorithms following DSM-5. The diagnosis of ODD was obtained annually. The

interviews in the first assessment gathered data from the first 3 years of life. ADHD, major

depression, any anxiety disorders (separation, generalized, social anxiety or specific phobias)

and comorbidity (ADHD, conduct disorder, major depression or any anxiety plus ODD) were

obtained at each age from 3 to 9 years old. Subthreshold ODD was defined as cases that did

not meet the threshold criteria of four symptoms for the diagnosis but presented impairment

or distress. Rowe's(18) ODD dimensions were used (*irritable* and *headstrong)*.

The *Strengths and Difficulties Questionnaire* (SDQ)(24) assesses emotional and behavioural

problems with 25 items with 3 response options organized in 5 scales. It was answered by the

parents and teachers. Cronbach's alpha for parents range from .55 (conduct) to .85

(hyperactivity) and for teachers from .69 (conduct) to .88 (total).

The *Children's Global Assessment Scale* (CGAS)(26) is a global measure of functional

impairment rated by the interviewer. Scale scores range from one (maximum impairment) to

100 (normal functioning). Scores above 70 indicate normal adaptation.

Children's Behavior Questionnaire Short Form and Very Short Form(27) measure reactive

and self-regulative temperament with 94 and 36 items respectively on a 7-point Likert-type

scale. These were answered by the parents when the children were 3, 4 and 5 years old (short

form) and 7 years old (very short form). The broad dimensions negative affectivity and

effortful control were considered. Cronbach's alpha in the sample ranged from .71 for

effortful control at age 7 to .85 for negative affectivity at age 5.

The *Behavior Rating Inventory of Executive Function preschool version* (BRIEF-P)(28),

answered by teachers when children were 3 years old, assesses behaviors reflecting the

executive functions in daily life. The broad dimension that combine inhibit (control of

impulses and behavior) and emotional control (appropriate modulation of emotional

responses) (ISCI) was used (Cronbach's alpha: .94).

The *Alabama Parenting Questionnaire-Preschool* (APQ-Pr)(29), measures parental practices

in three dimensions (24 items): positive discipline techniques, inconsistent parenting and

punitive parenting(30). They were obtained at ages 3 and 6. Cronbach's alpha for the three

dimensions was .75, .62 and .42 at age 3, and .74, .66 and .52 at age 6, respectively.

The *Adult Self-Report* (ASR)(31) assesses dimensional psychopathology (126 itemsI in

adults. The mothers answered the questionnaire when the children were 3 and 8 years old.

Internalizing and externalizing scale scores were analyzed (Cronbach's alpha .85 and .80

respectively at the last follow-up).

Patient and Public Involvement statement

Oppositional defiant disorder is a social problem and families and schools complain about how to manage disruptive behavior disorders at home and at the school. We wanted to investigate about the development of this problem to know the best developmental moments and their risk factors to help the families and the teachers to prevent oppositionality. Families and schools were freely and actively involved in the study. Families and schools were informed yearly of the results of the previous follow-up and were oriented about what to do to improve the behavior when necessary. Every 3 years they received a written report about the evolution and development of the child. Teachers received a 15 hours course about *How to manage disruptive behavior disorder at the school-room* at the beginning of different school levels (preschool -age 3-, elementary -ages 6 and 9).

Procedure

The project was approved by the Ethics Committee for Human and Animal Experimentation of the authors' institution. Families were recruited at the schools and gave written consent. The families who agreed to participate and met the screening criteria were contacted each year and interviewed at the school. Interviewers were trained and were blind to the screening group. All the interviews were audio-recorded and supervised. The data was collected between November-2009 and July-2016.

Statistical Analysis

The data was analyzed with Stata 15 for Windows. All analyses were weighted by the screening group membership in the sample design procedure. The incidence proportion was calculated for one-year time periods beginning at 4 years old by dividing the number of new cases of ODD (incident cases) by the number of children at risk, i.e. the number of cases at the beginning of the period excluding those who had previous diagnoses of ODD. This ratio is

also called Risk (R) and it estimates the 'probability of an event during a specified period of

time'(8). Cumulative risk estimates the risk of ODD from 0 years old to each time period;

because of the lost cases across the study, cumulative risk was computed by the product-limit

estimation(32) using the weighted annual risk.

The analysis of differences in psychopathology and functioning by age of onset of

ODD was made by ANOVA for quantitative outcomes and logistic regression for binary

outcomes. Age of onset was grouped into preschool (3-5) and school (6-9) periods. The group

without ODD was also considered and post-hoc comparisons corrected by Bonferroni for

multiple comparisons were estimated. Treatment for ODD at any time was introduced as

covariate.

To analyze the predictors of the risk of an ODD diagnosis, several Cox proportional

hazard regression models were estimated, grouping predictors (risk factors) by the

measurement instrument and adjusting estimates by sex and SES. Predictors were considered

as time dependent between ages 3 to 8 to benefit from the most recent available information.

As a consequence and because of the multiple-record structure of the data matrix (each child

had one data record for each follow-up period), the robust variance estimator(33) was used.

No competitive events were considered due to the high specificity of an ODD diagnosis and

to the characteristics of the sample, with neither deaths nor physical comorbidities that

prevented an ODD diagnosis. Proportional hazard assumption was verified by calculating the

significance value of the interaction between predictors and time. In the presence of

significant interaction, the hazard ratio for the involved predictor was obtained separately for

each year. For each Cox regression model, Harrell's C index(34) was calculated to evaluate

the adequacy of the predictions (values $\geq$ .70 are considered good).

RESULTS

Prevalence of ODD from 3 to 9 years old

Table 2 presents the number of children in the study, the number of ODD diagnoses and the prevalence for each age. Prevalence oscillated between 6.0% (age 3) and 8.8% (age 9).

First-Incidence and cumulative risk of ODD from 4 to 9 years old

The first three columns in Table 3 show the cases at risk (without an ODD diagnosis) at the beginning of each year period, the number of new cases diagnosed with ODD during that year and the incidence. The probability of the appearance of ODD showed a cubic shape, with risk increasing from age 4 to age 5 (R=2.7% to 4.4%), followed by a decrease until age 7 (R=1.9%) and a new increase at ages 8 and 9 (R=2.9%, 3.6%). The last column in Table 3 shows the cumulative risk of having a first ODD diagnosis up to 9 years old, which reached 21.9%.

Outcomes of age of onset of ODD

Table 4 shows the scores and percentages of psychopathology and functioning for children with onset of ODD at 3-5 and 6-9 years old and for those without ODD, as well as the multiple comparisons between the three groups. Children with onset at 3-5 years old scored higher on all the scales scores of parent's SDQ, higher conduct problems according to teachers, worse functioning and higher comorbidity in comparison to children without ODD. Children with onset of ODD at 6-9 years old scored higher on all the scales of parent's SDQ except prosocial, higher scores on peer problems and total according to teachers, and worse functioning in comparison with children without ODD. Children with onset of ODD at 3-5 years old presented higher comorbidity with anxiety problems in comparison with those

starting at 6-9, whereas children with onset of ODD at 6-9 years old presented higher

functional impairment than those with onset at 3-5 years old.

Risk factors of incident ODD diagnose from 3 to 9 years old

Hazard ratio (HR) for each risk factor with the 95% confidence interval and its *p* value

and Harrell's C for each model were calculated (See Supplementary Table 1). The hazard of

having an ODD diagnosis was increased by subthreshold ODD symptomatology (HR=6.3),

high scores on ODD dimensions of irritability (HR=1.6) and headstrong (HR=2.3),

comorbidity (HR=2.2), specifically of ADHD (HR=2.6), higher negative affectivity (HR=3.7

age 3 to HR=1.7 age 7), difficulties in inhibition and emotional control (HR=1.04), higher

scores in punitive parenting (HR=1.2) and mother's internalizing problems (HR=1.06).

DISCUSSION

To our knowledge this is the first study reporting on not only the one-year incidence of

ODD in a seven-year follow-up design covering ages 3 to 9 and the effects of different age

ranges of onset, but also their risk factors and the DSM-5 prevalence. We found that the

probability of the appearance of ODD shows a cubic shape with higher values for the

preschool period, a decrease at the start of childhood (ages 6 and 7) and another increase

when approaching puberty (ages 8 and 9). Prevalence was around 6-7% between ages 3 and 8,

increasing to 8.8% by age 9. An early onset of ODD is more closely associated with the

presence of comorbidity, but the functional impairment of those with later onset is most

marked. Risk factors of incicende were identified.

Throughout development prevalence was high and very stable (6-7%), with the highest

value at 9 years old. These percentages indicate the need to allocate resources such as services

and training to the parents, teachers and professionals involved with the children in these age ranges that have already developed the disorder.

2.7 and 4.4 out of 100 preschoolers aged 4 and 5, respectively, and between 1.9 and 3.6 out of 100 children aged 6 to 9 will develop a first episode of ODD in one year. It is remarkable that at the end of the follow-ups the cumulative risk was high, indicating that up to 9 years old the risk of presenting ODD is 21.9%. This risk is highest in the preschool period, which cumulates 12.6% of the risk, the remaining 9.3% occurring in childhood. These values are noteworthy in terms of public mental health indicators if one considers the short-term impact ODD has on the lives of children, families, teachers and schools(6), as well as the long-term effects until adulthood(7). Specifically, these results point to the need to pay attention to the preschool period if the goal is to prevent ODD. On the one hand, preschool age is when the child is acquiring important skills related to ODD, such as self-regulation and executive functioning, and when parents adjust their parenting practices(35). It is important to intervene in this period when the early signs of dysfunction become apparent. On the other hand, programmes that have been shown to effectively treat ODD(36) (37) (38) and prevent it(39) (40) are currently available.

An early age of onset has typically been associated with worse mental health outcomes(11). This is also true for ODD regarding comorbidity. The risk of ADHD, anxiety or depression in children who debut ODD at preschool age multiplies by 3.4 to 5.9 compared to children without ODD. Comparing early versus later onset, early onset multiplies by almost 4 times the risk of developing anxiety. One of the contributions of studying age of onset is to have available information for targeting prevention that focuses on early intervention in incipient mental disorders and on primary prevention of secondary disorders(11). Thus, our results once again suggest the need to intervene at early ages. This implication is also supported by the finding that for those starting later (ages 6-9), the impairment in functioning

is more severe. Therefore, paying attention to prodromal indicators and risk factors to prevent the full development of ODD is crucial.

Regarding risk factors, our goal was to confirm the risk of first onset of ODD using some of the main risk factors reported previously in the literature. No previous studies have been carried out with incident cases. The strength of the association for some of the predictors is remarkable. We found that pre-morbid forms of ODD (subthreshold, high scores in the ODD dimensions irritability and headstrong) were the strongest predictor of onset of full ODD. Identifying pre-morbid cases is of great value for the indicated prevention of ODD, given that the group at risk presents objective markers (ODD symptoms). Similarly, children with other psychopathology, and specifically ADHD, and individual characteristics, such as difficulties in inhibit-emotional control are also at risk of onset of ODD. Also, our results indicate that difficulties regulating negative emotions are at a higher risk of ODD onset, especially from very early ages, while the risk diminishes with age. Last, unsupportive environments, such as punitive parenting practices and maternal internalizing problems, predicted the emergence of an ODD diagnosis, which is also in line with previous literature(13, 41). Predictive capability assessed by Harrell's C was generally low to moderate. However, it is necessary to consider the low number of predictors included in each model.

Strengths of the study are that the diagnostic information was obtained via semi-structured interviews based on DSM-5 criteria, the length of the follow-up period (7 years), the inclusion of two different developmental stages, preschool and childhood, and the fact that the estimates of incidence were not overestimated, given that previous diagnoses until age 3 were also made. Age of onset studies have been carried out mostly through retrospective design, which is a limitation. We studied age of onset through a prospective design. Furthermore, the information on risk factors was obtained from parents and teachers.

However, some limitations must be considered when interpreting the results. The diagnostic

information, based on data from just one source, the parents, and the lower participation of

low SES families may have led to bias in the estimates. Also, some of the scales of the APQ-

Pr presented low internal consistency and the results should thus be interpreted with caution.

Synthesizing, oppositional defiant disorder is one of the most prevalent disorders in

our society. It has important consequences in the development of the child and in the

functioning of the family. It starts very early in life but we do not know how many new cases

appear every year, nor the consequences it has depending on the age of onset. Our study

reports that the probability of appearance of oppositional defiant disorders is highest by age 5

and, afterwards, by age 9, when approaching to puberty. Most of the new cases of

oppositional disorder appeared in preschool age (12.6%). By age 9 there is a cumulative risk

of new onset of 21.9%. Early onset at preschool age is associated with comorbidity with

anxiety and depression; childhood onset is associated with higher functional impairment.

These results indicate the burden of oppositional disorder for public health and point to the

need of focusing in preschool age for preventive purposes. To allocate resources in this

developmental period and paying attention to prodromal indicators and risk factors to prevent

the full development of ODD is crucial.

Contributorship statement

LE designed the study and wrote the paper with JBN. JBN analyzed data. JMD contributed to

data analysis. N. de la Osa and EP collaborated in the writing editing of the manuscript. All

the authors contributed reviewing the final version of the manuscript.

Availability of data and materials

Data cannot be publicly available due to ethical restrictions protecting the confidentiality of

the families involved. Data are available to interested researchers after signing a consent of

confidentiality form as the authors had previously signed to obtain the data from the families

of the sample. Researchers must be working in clinical child psychology in a public funded

project. To request the anonymous data, please contact the corresponding author.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical

standards of the relevant national and institutional committees on human experimentation and

with the Helsinki Declaration of 1975, as revised in 2008.

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Conflict of interests

The authors have no conflicts of interests.

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Table 1

Demographic Characteristics of the Sample at age 3 (N = 622)

Age (mean; *SD*)	3.8 (.33)
Sex; *n (%)*	
Male	311 (50.0)
Race/ethnicity; *n (%)*	
Non-Hispanic White	557 (89.5)
Hispanic-American	46 (7.4)
Other	19 (3.1)
SES; n *(%)*	
High	205 (33.0)
Middle	280 (45.0)
Low	137 (22.0)

Table 2

DSM-5 ODD Prevalence from 3 to 9 years-old.

Age (years-old)	Total cases	ODD cases	Prevalence* %
3	622	65	6.03
4	604	63	7.08
5	535	46	7.09
6	509	47	7.04
7	456	41	6.99
8	469	35	6.09
9	418	40	8.83

*Weighted by screen-positive or screen-negative membership: number of children with ODD divided by the total sample size at that age.

Table 3

ODD One-Year First-Incidence and Cumulative Risk from 0 to 9 years-old.

Age (years-old)	Cases at risk	Incident ODD cases[a]	First ODD diagnosis	
			Risk[b] %	Cumulative Risk[c] (%)
0 to 3				6.0
4	541	23	2.71	8.6
5	463	20	4.39	12.6
6	419	13	2.65	14.9
7	367	10	1.88	16.5
8	373	11	2.92	18.9
9	325	13	3.61	21.9

[a]Incident cases (after excluding children with previous diagnoses of ODD)

[b]Weighted by screen-positive or screen-negative membership

[c]Computed by product-limit estimation using weighted annual risk

Table 4

Outcome of Age of Onset on Psychopathology and Functioning (n = 461).

	No ODD (*n* = 305)	Age onset 3-5 years-old (*n* = 113)	Age onset 6-9 years-old (*n* = 43)	3-5 vs No ODD*		6-9 vs No ODD*		6-9 vs 3-5*	
	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	Mean Difference	*p*	Mean Difference	*p*	Mean Difference	*p*
SDQ- Parent									
Emotional	1.01 (0.88)	1.92 (1.52)	2.18 (1.42)	0.81	**<.005**	1.01	**<.005**	0.20	.430
Conduct	1.18 (0.84)	3.00 (1.54)	2.87 (1.32)	1.68	**<.005**	1.44	**<.005**	-0.24	.436
Hyperactivity	3.01 (2.08)	4.28 (2.36)	4.95 (2.33)	1.03	**.001**	1.58	**<.005**	0.55	.229
Peer	0.69 (0.75)	1.35 (1.24)	1.65 (1.17)	0.60	**<.005**	0.87	**<.005**	0.27	.232
Prosocial	1.47 (1.04)	2.14 (1.22)	1.90 (1.57)	0.58	**.001**	0.29	.323	-0.29	.360
Total	5.89 (3.29)	9.90 (5.33)	11.64 (3.97)	3.45	**<.005**	4.89	**<.005**	1.44	.087
SDQ Teacher									
Emotional	1.28 (1.02)	1.84 (1.44)	2.14 (1.89)	0.35	.056	0.58	.073	0.23	.530
Conduct	1.22 (1.21)	2.00 (1.81)	2.25 (1.92)	0.53	**.011**	0.61	.090	0.08	.831
Hyperactivity	2.86 (2.29)	3.71 (2.32)	4.39 (2.90)	0.47	.105	1.02	.062	0.55	.318
Peer	1.11 (1.01)	1.48 (1.19)	1.87 (1.36)	0.19	.130	0.52	**.015**	0.33	.163
Prosocial	2.43 (1.43)	3.05 (1.78)	3.28 (2.16)	0.30	.166	0.43	.245	0.13	.744
Total	6.47 (4.26)	8.68 (5.20)	10.46 (6.40)	1.15	.051	2.57	**.019**	1.42	.220
CGAS	78.33 (5.73)	66.99 (7.60)	59.03 (7.24)	-9.59	**<.005**	-16.64	**<.005**	-7.05	**<.005**
DSM-5	%	%	%	OR	*p*	OR	*p*	OR	*p*
ADHD	15.5%	51.8%	39.3%	4.50	**<.005**	2.43	.041	0.54	.170
Major depression	1.5%	9.4%	7.1%	5.86	**.004**	4.35	.188	0.74	.751
Any Anxiety disorder	26.0%	57.8%	26.7%	3.43	**<.005**	0.89	.817	0.26	**.011**

* Comparison between ages of first ODD diagnose are adjusted by having or not ODD treatment

In bold significant *p* values after Bonferroni correction for multiple comparison

Table 1 online

Predictors of incident cases (n = 539)

	Age	HR*	p	95% CI	Harrell's C
ODD Subthreshold		6.27	**<.001**	3.85 ; 10.21	.70
ODD Irritability		1.56	**.007**	1.13 ; 2.12	.76
ODD Headstrong		2.33	**<.001**	1.84 ; 2.96	
Comorbidity (DSM5)		2.21	**.001**	1.39 ; 3.53	.58
DSM-5					
ADHD		2.64	**.002**	1.42 ; 4.93	.53
Any Anxiety		1.01	.982	0.40 ; 2.54	
Children's Behavior Questionnaire					
Negative affectivity	3	3.73	**<.001**	2.21 ; 6.29	
	4	3.06	**<.001**	2.01 ; 4.64	
	5	2.50	**<.001**	1.80 ; 3.49	
	6	2.05	**<.001**	1.55 ; 2.71	.69
	7	1.68	**<.001**	1.27 ; 2.23	
	8	1.38	.061	0.99 ; 1.93	
Effortful Control		0.88	.457	0.64 ; 1.22	
BRIEF ISCI		1.04	**<.001**	1.02 ; 1.07	.61
Alabama Parenting Questionnaire					
Positive parenting		1.01	.695	0.96 ; 1.07	
Inconsistency		1.00	.997	0.94 ; 1.07	.62
Punitive parenting		1.22	**.001**	1.08 ; 1.38	
Adult Self-Report (mother)					
Internalizing		1.06	**.002**	1.02 ; 1.10	.63
Externalizing		0.99	.991	0.94 ; 1.05	

*Weighted by screen-positive or screen-negative membership and adjusted by sex and socioeconomic status;

HR: Hazard ratio; CI: Confidence interval; BRIEF ISCI: BRIEF Inhibit and Emotional Control

In bold *p*-values < .05.

Risk factors of a first ODD diagnose from 3 to 9 years old

Table 5 presents the hazard ratio (HR) for each risk factor with the 95% confidence

interval and its *p* value and Harrell's C for each model.

First, the variables related to ODD symptomatology were studied to know how pre-

morbid forms of ODD are related to first-incidence. The hazard of having an ODD diagnosis

was multiplied by 6.27 if there was subthreshold ODD at any of the follow-ups. In the same

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line, higher scores in the ODD dimensions of irritability and headstrong increased the risk of

the incidence of ODD, each point of the dimension scores multiplying this risk by 1.56 for

irritability and 2.33 for headstrong. These models obtained a moderate to good level of

adequacy for the predictions (Harrell's C=.70 and .76).

Second, we studied how other psychopathologies predicted the risk of a first ODD

diagnosis. The presence of comorbidity (HR=2.21), and specifically of ADHD (HR=2.64),

significantly increased the risk of new cases of ODD. These models obtained a poor level of

adequacy for the predictions (C=.58 and .53).

Third, the individual characteristics of the child, such as temperament and executive

functioning, were studied as risk factors for the appearance of ODD. As the effect of CBQ

negative affect did not meet the proportional hazard assumption, a HR was obtained for each

year. The hazard of ODD increased with higher negative affectivity scores and this effect was

significant and descending from ages 3 to 7 (HR=3.73 age 3 to HR=1.68 age 7) and not

significant thereafter. For effortful control, the proportionality assumption was met, but there

was no significant association with ODD. Difficulties in executive functioning in the areas of

inhibition and emotional control (ISCI) were associated with risk of ODD (HR=1.04). The

accuracy of the predictions was moderate-poor for these models (C=.69 and .61).

Last, we studied the influence of environmental variables. Higher scores in punitive

parenting (HR=1.22) and mother's internalizing problems (HR=1.06) increased the risk of

ODD. The adequacy of the predictions was poor for both models (C=.62 and .61).

2

BMJ Open

First-Incidence, Age of Onset Outcomes and Risk Factors of Onset of DSM-5 Oppositional Defiant Disorder: A cohort study of Spanish children from ages 3 to 9

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Running Head: INCIDENCE OF ODD

First-Incidence, Age of Onset Outcomes and Risk Factors of Onset of DSM-5

Oppositional Defiant Disorder: A cohort study of Spanish children from ages 3 to 9

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ABSTRACT

Objective To examine the one-year first-incidence and prevalence of oppositional defiant

disorder (ODD), the outcomes on psychopathology and functioning by age of onset and the

risk factors of onset of ODD from ages 3 to 9 in children from the Spanish general population.

Design Longitudinal with 7 follow-ups and double cohort (ODD and non-ODD children).

Setting General population of preschool and elementary school children in Barcelona (Spain).

Participants On a first phase the parent-rated Strengths and Difficulties Questionnaire

conduct problems scale plus oppositional defiant disorder DSM-IV symptoms were used to

screen for behavioral problems. The second phase sample size contained 622 cases at age 3

and at age 9 418 remained in the study.

Results The probability of the onset of ODD showed increasing values at ages 4 (R =2.7%)

and 5 years (R=4.4%). These values decreased until age 7 (R=1.9%) and increased again until

age 9 (R=3.6%). Up to 9 years old the cumulative risk of new cases of ODD was 21.9%. Early

onset was associated with a higher risk of comorbidity and later onset with higher functional

impairment. Subthreshold ODD, high scores in irritability and headstrong dimensions, ADHD

and other comorbidity, negative affectivity until age 7, difficulties in inhibit and emotional

control, punitive parenting and maternal internalizing problems were risk factors of a first

episode of ODD during this seven-year period.

Conclusions The risk of new cases of ODD in the general population at preschool age and

during childhood is high. Preschool age is a target period for preventive interventions.

Identified risk factors are objectives for targeted and indicated interventions.

Strengths and limitations of the study

- Strengths of the study are that the diagnostic information was obtained via semi-structured interviews based on DSM-5 criteria, the length of the follow-up period (7 years), the inclusion of two different developmental stages, preschool and childhood, and the fact that the values of incidence were not overestimated, given that previous diagnoses until age 3 were also made. Also age of onset through a prospective design. Furthermore, the information on risk factors was obtained from parents and teachers.

- A strength of data analysis is the consideration of risk factors in Cox regression models as time dependent covariates instead of fixed covariates, as well as the estimation of different coeficients for each age when the proportional hazars assumption was violated.

- The diagnostic information, based on data from just one source, the parents, and the lower participation of low SES families may have led to bias in the estimates. The internal consistency of some parenting scales makes that parenting practices results should be interpreted with caution.

- A limitation of data analysis is grouping ages (3-5 and 6-9) in the analysis of the influence of ODD age of onset on psychopathology and functioning. This was necessary because, otherwise, there were not enough incident ODD cases in each age.

FIRST-INCIDENCE, AGE OF ONSET OUTCOMES AND RISK FACTORS OF ONSET OF DSM-5 OPPOSITIONAL DEFIANT DISORDER: A COHORT STUDY OF SPANISH CHILDREN FROM AGES 3 TO 9

According to epidemiological studies the proportion of children and adolescents with mental health problems is 13.4%(1). These disorders are stable and continue into later life with adverse adults outcomes(2). Therefore, childhood is a target period for the early identification and prevention of mental disorders.

Oppositional defiant disorder (ODD), a pattern of negativistic, defiant, disobedient and hostile behaviour, is one of the most prevalent disorders from preschool age to adulthood(3)(4). The pooled prevalence is 3.6% up to age 18(1). ODD is accompanied by various concurrent disorders (attention deficit/hyperactivity disorder-ADHD), successive comorbidity (conduct disorder, anxiety, depression, substance use)(5,6) and functional impairment (7,8). Symptomatology is stable and sufferers have difficulties in the transition to adulthood(9). The amount of children and families affected and the severe consequences that compromise healthy mental development underscore the need to know when the first onset occurs and the factors that predict this onset in order to plan appropriate preventive strategies.

Currently, we know how many children in the population are affected by ODD at a given point in time; that is, the prevalence, a measure of the status of the disease. We do not know, however, how many new cases appear at different developmental stages; that is, incidence, a measure of newly occurring cases of the disease during a specific developmental period(10). Because there is often a low number of incident cases, incidence studies require cohort designs with large size samples. Literature shows that there is a dearth of studies about the incidence of psychiatric disorders in childhood and adolescence. The available data on ODD mostly focus on adolescents and youths. Roberts(11) reported that the risk of new cases of ODD for adolescents in a 12-month period was 1.56% and Benjet(12) found a 5% 8-year

incidence for 19- to 26-year-old youth. There are no studies on the incidence of ODD during preschool and childhood. Neither do we know the differential consequences of the disorder according to age of onset. Literature on general mental disorders has reported that early onset is associated with greater severity, persistence and lack of response to treatment(13). Age of onset is an important data to advise on mental health policies(14).

Several risk factors have been reported in the literature on ODD. Child risk factors include genetic influences(15), difficult temperament(16), difficulties in processing social information(17), sex(18) and ADHD(19). The contextual factors reported include socioeconomic status, parenting practices, parental psychopathology, family conflict and poor attachment(15,20). Incidence figures, which report on new cases of disease, are more useful for identifying risk factors than prevalence studies, which include both chronic and new cases(21). No previous studies have examined the risk factors of ODD by considering new cases. Only Roberts(11) adopted this approach in adolescents, reporting that a younger age, poor family satisfaction, passive coping and low mastery, school and economic stress and poor relations with parents were predictors of incident cases of ODD.

Furthermore, ODD is a continuous disorder that starts early in life and persists into adulthood(9). It is therefore imperative to know for prevention purposes how the early manifestations of ODD symptomatology affect the definite appearance of the full disorder. Several dimensions of ODD have been identified to explain its underlying structure: irritable (including loses temper, angry and touchy); headstrong (argues, defies, annoys, blames) and hurtful (spiteful-vindictive)(22). Rowe(20) showed how ODD dimensions predict full ODD diagnosis. Moreover, the literature has shown that subthreshold conditions are risk factors for developing similar (homotypic) or different (heterotypic) full-syndrome(23) and that they constitute a major public mental health burden(24).

The objective was to study annually the proportion of incident cases of ODD from ages 3 to 9 (preschool through childhood), to ascertain the differential outcomes by age of onset and to test if previously reported risk factors associated with ODD are prospective risk factors of incident cases at these developmental stages.

METHOD

Participants

The initial sample consisted of 2,283 children randomly selected from early childhood schools in Barcelona (Spain)(25). A two-phase design was employed. In the first-phase of sampling, 1,341 families (58.7%) agreed to participate (33.6% high socioeconomic status (SES), 43.1% middle and 23.3% low; 50.9% boys). To ensure that children with possible behavioral problems participated, the parent-rated Strengths and Difficulties Questionnaire (SDQ[3-4]) conduct problems scale(26) plus ODD DSM-IV symptoms were used to screen. Two groups were considered: screen-positive (all children with SDQ scores ≥4, percentile 90, or with a positive response to any of the eight DSM-IV ODD symptoms) and screen-negative (a random group comprising 28% of children who did not reach the positive threshold). The sample size was determined for detecting OR ≥ 1.8 between psychopathology and risk factors, using a test of hypothesis for risk α = .05 and power of .80. As the planned follow-up was 12 years long, the sample size was increased 50% for losses.

Children of each classroom were alphabetically numbered and did not contain the name of the child nor the school. Those scoring under the cut-off were randomly permutated using SPSS random number generator, and the first 30% was selected. The final sample for the follow-ups (second-phase) included 622 children (Figure 1). The screen-positive group comprised 417 children (49.4% boys) and the screen-negative group 205 children (51.2%, boys). No differences in sex (χ^2 =0.07; p =.793) or type of school (χ^2 =0.72; p =.396) were

found on comparing completers and drop-outs during the seven years of annual follow-ups. However, the SES of those leaving the study until age 9 was lower (χ^2=20.89; p <.001).

From the initial 622 children, 65 who presented an ODD diagnosis at the start of the study (age 3) and 18 who left the study at the second follow-up (age 4) were excluded for the analysis of risk factors because lack of information (N =539). Decrements in sample size at successive follow-ups were either due to attrition or to the exclusion of children who had already presented a first ODD diagnosis. Demographic characteristics are shown in Table 1.

Measures

Diagnostic Interview of Children and Adolescents for Parents of Preschool Children (DICA-PPC)

The DICA-PPC(27) is a computerised semi-structured interview which generates diagnoses through algorithms following DSM-5. The diagnosis of ODD was obtained annually. The interviews in the first assessment gathered data from the first 3 years of life. ADHD, major depression, any anxiety disorders (separation, generalized, social anxiety or specific phobias) and comorbidity (ADHD, conduct disorder, major depression or any anxiety plus ODD) were obtained at each age from 3 to 9 years old. Subthreshold ODD was defined as cases that did not meet the threshold criteria of four symptoms for the diagnosis but presented impairment or distress. Rowe's(20) ODD dimensions were used (*irritable* and *headstrong)*.

The *Strengths and Difficulties Questionnaire* (SDQ)(26) assesses emotional and behavioural problems with 25 items with 3 response options organized in 5 scales. It was answered by the parents and teachers. Cronbach's alpha for parents range from .55 (conduct) to .85 (hyperactivity) and for teachers from .69 (conduct) to .88 (total).

The *Children's Global Assessment Scale* (CGAS)(28) is a global measure of functional

impairment rated by the interviewer. Scale scores range from one (maximum impairment) to

100 (normal functioning). Scores above 70 indicate normal adaptation.

Children's Behavior Questionnaire Short Form and Very Short Form(29) measure reactive

and self-regulative temperament with 94 and 36 items respectively on a 7-point Likert-type

scale. These were answered by the parents when the children were 3, 4 and 5 years old (short

form) and 7 years old (very short form). The broad dimensions negative affectivity and

effortful control were considered. Cronbach's alpha in the sample ranged from .71 for

effortful control at age 7 to .85 for negative affectivity at age 5.

The *Behavior Rating Inventory of Executive Function preschool version* (BRIEF-P)(30),

answered by teachers when children were 3 years old, assesses behaviors reflecting the

executive functions in daily life. The broad dimension that combine inhibit (control of

impulses and behavior) and emotional control (appropriate modulation of emotional

responses) (ISCI) was used (Cronbach's alpha: .94).

The *Alabama Parenting Questionnaire-Preschool* (APQ-Pr)(31), measures parental practices

in three dimensions (24 items): positive discipline techniques, inconsistent parenting and

punitive parenting(32). They were obtained at ages 3 and 6. Cronbach's alpha for the three

dimensions was .75, .62 and .42 at age 3, and .74, .66 and .52 at age 6, respectively.

The *Adult Self-Report* (ASR)(33) assesses dimensional psychopathology (126 itemsI in

adults. The mothers answered the questionnaire when the children were 3 and 8 years old.

Internalizing and externalizing scale scores were analyzed (Cronbach's alpha .85 and .80

respectively at the last follow-up).

Patient and Public Involvement statement

Oppositional defiant disorder is a social problem and families and schools complain

about how to manage disruptive behavior disorders at home and at the school. We wanted to

investigate about the development of this problem to know the best developmental moments

and their risk factors to help the families and the teachers to prevent oppositionality. Families

and schools were freely and actively involved in the study. Families and schools were

informed yearly of the results of the previous follow-up and were oriented about what to do to

improve the behavior when necessary. Every 3 years they received a written report about the

evolution and development of the child. Teachers received a 15 hours course about *How to*

manage disruptive behavior disorder at the school-room at the beginning of different school

levels (preschool -age 3-, elementary -ages 6 and 9).

Procedure

The project was approved by the Ethics Committee for Human and Animal

Experimentation of the Universitat Autònoma de Barcelona. Families were recruited at the

schools and gave written consent. The families who agreed to participate and met the

screening criteria were contacted each year and interviewed at the school. Interviewers were

trained and were blind to the screening group. All the interviews were audio-recorded and

supervised. The data was collected between November-2009 and July-2016.

Statistical Analysis

The data was analyzed with Stata 15 for Windows. All analyses were weighted by the

screening group membership in the sample design procedure. Cases with missing data were

excluded separately for each analysis (pairwise deletion). The incidence proportion was

calculated for one-year time periods beginning at 4 years old by dividing the number of new

cases of ODD (incident cases) by the number of children at risk, i.e. the number of cases at

the beginning of the period excluding those who had previous diagnoses of ODD. This ratio is

also called Risk (R) and it estimates the 'probability of an event during a specified period of

time'(10). Cumulative risk estimates the risk of ODD from 0 years old to each time period;

because of the lost cases across the study, cumulative risk was computed by the product-limit

estimation(34) using the weighted annual risk.

The analysis of differences in psychopathology and functioning by age of onset of

ODD was made by ANOVA for raw scores of quantitative outcomes and logistic regression

for binary outcomes. Age of onset was grouped into preschool (3-5) and school (6-9) periods.

The group without ODD was also considered and post-hoc comparisons corrected by

Bonferroni for multiple comparisons were estimated. Treatment for ODD at any time was

introduced as covariate to adjust for confounding effects.

To analyze the predictors of the risk of an ODD diagnosis, several Cox proportional

hazard regression models were estimated, grouping predictors (risk factors) by the

measurement instrument and adjusting estimates by sex and SES. Predictors were considered

as time dependent between ages 3 to 8 to benefit from the most recent available information.

As a consequence and because of the multiple-record structure of the data matrix (each child

had one data record for each follow-up period), the robust variance estimator(35) was used.

No competitive events were considered due to the high specificity of an ODD diagnosis and

to the characteristics of the sample, with neither deaths nor physical comorbidities that

prevented an ODD diagnosis. Proportional hazard assumption was verified by calculating the

significance value of the interaction between predictors and time. In the presence of

significant interaction, the hazard ratio (HR) for the involved predictor was obtained

separately for each year. For each Cox regression model, Harrell's C index(36) was calculated

to evaluate the adequacy of the predictions (values ≥ .70 are considered good).

RESULTS

Prevalence of ODD from 3 to 9 years old

Table 2 presents the number of children in the study, the number of ODD diagnoses

and the prevalence for each age. Prevalence oscillated between 6.0% (age 3) and 8.8% (age

9).

First-Incidence and cumulative risk of ODD from 4 to 9 years old

The first three columns in Table 3 show the cases at risk (without an ODD diagnosis)

at the beginning of each year period, the number of new cases diagnosed with ODD during

that year and the incidence. The probability of the appearance of ODD showed a cubic shape,

with risk increasing from age 4 to age 5 (R=2.7% to 4.4%), followed by a decrease until age 7

(R=1.9%) and a new increase at ages 8 and 9 (R=2.9%, 3.6%). The last column in Table 3

shows the cumulative risk of having a first ODD diagnosis up to 9 years old, which reached

21.9%.

Outcomes of age of onset of ODD

Table 4 shows the scores and percentages of psychopathology and functioning for

children with onset of ODD at 3-5 and 6-9 years old and for those without ODD, as well as

the multiple comparisons between the three groups with the mean difference (MD) or the

odds ratio (OR) and their 95% confidence intervals. Children with onset at 3-5 years old

scored higher on all the scales scores of parent's SDQ (MD between 0.58 for prosocial and

1.68 for conduct problems), on conduct problems according to teachers (MD = 0.53), and

presented worse functioning (MD = -9.59) and higher comorbidity (OR between 3.43 for any anxiety and 5.86 for major depression) in comparison to children without ODD. Children with onset of ODD at 6-9 years old scored higher on all the scales of parent's SDQ except prosocial (MD between 0.87 for peer and 1.58 for hyperactivity), on peer problems (MD = 0.52) and total according to teachers, and presented worse functioning (MD = -16.64) in comparison with children without ODD. There were not differences in any SDQ score between preschooler and late ODD onset. Children with onset of ODD at 3-5 years old presented higher comorbidity with anxiety problems in comparison with those starting at 6-9 (OR = 0.26), whereas children with onset of ODD at 6-9 years old presented higher functional impairment than those with onset at 3-5 years old (MD = -7.05).

Risk factors of incident ODD diagnose from 3 to 9 years old

Hazard ratio (HR) for each risk factor with the 95% confidence interval, its *p* value and Harrell's C for each model were calculated (See Supplementary Table 1). The hazard of having an ODD diagnosis was increased by subthreshold ODD symptomatology (HR=6. 27, 95% CI 3.85 to 10.21), high scores on ODD dimensions of irritability (HR=1.56, 95% CI 1.13 to 2.12) and headstrong (HR=2.33, 95% CI 1.84 to 2.96), comorbidity (HR=2.21, 95% CI 1.13 to 3.53), specifically of ADHD (HR=2.64, 95% CI 1.42 to 4.93), higher negative affectivity (HR=3.73, 95% CI 2.21 to 6.29 at age 3 to HR=1.68, 95% CI 1.27 to 2.23 at age 7), difficulties in inhibition and emotional control (HR=1.04, 95% CI 1.02 to 1.07), higher scores in punitive parenting (HR=1.22, 95% CI 1.08 to 1.38) and mother's internalizing problems (HR=1.06, 95% CI 1.02 to 1.10).

DISCUSSION

To our knowledge this is the first study reporting on not only the one-year incidence of

ODD in a seven-year follow-up design covering ages 3 to 9 and the effects of different age

ranges of onset, but also their risk factors and the DSM-5 prevalence. We found that the

probability of the appearance of ODD shows a cubic shape with higher values for the

preschool period, a decrease at the start of childhood (ages 6 and 7) and another increase

when approaching puberty (ages 8 and 9). Prevalence was around 6-7% between ages 3 and 8,

increasing to 8.8% by age 9. An early onset of ODD is more closely associated with the

presence of comorbidity, but the functional impairment of those with later onset is most

marked. Risk factors of incidence were identified.

Throughout development prevalence was high and very stable (6-7%), with the highest

value at 9 years old. These percentages indicate the need to allocate resources such as services

and training to the parents, teachers and professionals involved with the children in these age

ranges that have already developed the disorder.

2.7 and 4.4 out of 100 preschoolers aged 4 and 5, respectively, and between 1.9 and

3.6 out of 100 children aged 6 to 9 will develop a first episode of ODD in one year. It is

remarkable that at the end of the follow-ups the cumulative risk was high, indicating that up

to 9 years old the risk of presenting ODD is 21.9%. This risk is highest in the preschool

period, which cumulates 12.6% of the risk, the remaining 9.3% occurring in childhood. These

values are noteworthy in terms of public mental health indicators if one considers the short-

term impact ODD has on the lives of children, families, teachers and schools(8), as well as the

long-term effects until adulthood(9). Specifically, these results point to the need to pay

attention to the preschool period if the goal is to prevent ODD. On the one hand, preschool

age is when the child is acquiring important skills related to ODD, such as self-regulation and

executive functioning, and when parents adjust their parenting practices(37). It is important to

intervene in this period when the early signs of dysfunction become apparent. On the other

hand, programmes that have been shown to effectively treat ODD(38,39,40) and prevent it(41,42) are currently available.

An early age of onset has typically been associated with worse mental health outcomes(13). This is also true for ODD regarding comorbidity. The risk of ADHD, anxiety or depression in children who debut ODD at preschool age multiplies by 3.4 to 5.9 compared to children without ODD. Comparing early versus later onset, early onset multiplies by almost 4 times the risk of developing anxiety. One of the contributions of studying age of onset is to have available information for targeting prevention that focuses on early intervention in incipient mental disorders and on primary prevention of secondary disorders(13). Thus, our results once again suggest the need to intervene at early ages. This implication is also supported by the finding that for those starting later (ages 6-9), the impairment in functioning is more severe. Therefore, paying attention to prodromal indicators and risk factors to prevent the full development of ODD is crucial.

Regarding risk factors, our goal was to confirm the risk of first onset of ODD using some of the main risk factors reported previously in the literature. No previous studies have been carried out with incident cases. The strength of the association for some of the predictors is remarkable. We found that pre-morbid forms of ODD (subthreshold, high scores in the ODD dimensions irritability and headstrong) were the strongest predictor of onset of full ODD. Identifying pre-morbid cases is of great value for the indicated prevention of ODD, given that the group at risk presents objective markers (ODD symptoms). Similarly, children with other psychopathology, and specifically ADHD, and individual characteristics, such as difficulties in inhibit-emotional control are also at risk of onset of ODD. Also, our results indicate that difficulties regulating negative emotions are at a higher risk of ODD onset, especially from very early ages, while the risk diminishes with age. Last, unsupportive environments, such as punitive parenting practices and maternal internalizing problems,

predicted the emergence of an ODD diagnosis, which is also in line with previous

literature(15,43). Predictive capability assessed by Harrell's C was generally low to moderate.

However, it is necessary to consider the low number of predictors included in each model.

Strengths of the study are that the diagnostic information was obtained via semi-structured interviews based on DSM-5 criteria, the length of the follow-up period (7 years), the inclusion of two different developmental stages, preschool and childhood, and the fact that the estimates of incidence were not overestimated, given that previous diagnoses until age 3 were also made. Age of onset studies have been carried out mostly through retrospective design, which is a limitation. We studied age of onset through a prospective design. Furthermore, the information on risk factors was obtained from parents and teachers. However, some limitations must be considered when interpreting the results. The diagnostic information, based on data from just one source, the parents, and the lower participation of low SES families may have led to bias in the estimates. Also, some of the scales of the APQ-Pr presented low internal consistency and the results should thus be interpreted with caution.

Synthesizing, oppositional defiant disorder is one of the most prevalent disorders in our society. It has important consequences in the development of the child and in the functioning of the family. It starts very early in life but we do not know how many new cases appear every year, nor the consequences it has depending on the age of onset. Our study reports that the probability of appearance of oppositional defiant disorders is highest by age 5 and, afterwards, by age 9, when approaching to puberty. Most of the new cases of oppositional disorder appeared in preschool age (12.6%). By age 9 there is a cumulative risk of new onset of 21.9%. Early onset at preschool age is associated with comorbidity with anxiety and depression; childhood onset is associated with higher functional impairment. These results indicate the burden of oppositional disorder for public health and point to the need of focusing in preschool age for preventive purposes. To allocate resources in this

developmental period and paying attention to prodromal indicators and risk factors to prevent

the full development of ODD is crucial. Our results are generalizable to Spanish children

mostly from mean and high-mean socioeconomic levels until age 9.

Contributorship statement

LE designed the study and wrote the paper with JBN. JBN analyzed data. JMD contributed to

data analysis. N. de la O and EP collaborated in the writing editing of the manuscript. All the

authors contributed reviewing the final version of the manuscript.

Availability of data and materials

Data cannot be publicly available due to ethical restrictions protecting the confidentiality of

the families involved. Data are available to interested researchers after signing a consent of

confidentiality form as the authors had previously signed to obtain the data from the families

of the sample. Researchers must be working in clinical child psychology in a public funded

project. To request the anonymous data, please contact the corresponding author.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical

standards of the relevant national and institutional committees on human experimentation and

with the Helsinki Declaration of 1975, as revised in 2008.

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Conflict of interests

The authors have no conflicts of interests.

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Table 1

Demographic Characteristics of the Sample at age 3 (N = 622)

Age (mean; *SD*)	3.8 (.33)
Sex; *n (%)*	
Male	311 (50.0)
Race/ethnicity; *n (%)*	
Non-Hispanic White	557 (89.5)
Hispanic-American	46 (7.4)
Other	19 (3.1)
SES; n *(%)*	
High	205 (33.0)
Middle	280 (45.0)
Low	137 (22.0)

Table 2

DSM-5 ODD Prevalence from 3 to 9 years-old.

Age (years-old)	Total cases	ODD cases	Prevalence* %
3	622	65	6.03
4	604	63	7.08
5	535	46	7.09
6	509	47	7.04
7	456	41	6.99
8	469	35	6.09
9	418	40	8.83

*Weighted by screen-positive or screen-negative membership: number of children with ODD divided by the total sample size at that age.

Table 3

ODD One-Year First-Incidence and Cumulative Risk from 0 to 9 years-old.

Age (years-old)	Cases at risk	First ODD diagnosis		
		Incident ODD cases[a]	Risk[b] %	Cumulative Risk[c] (%)
0 to 3				6.0
4	541	23	2.71	8.6
5	463	20	4.39	12.6
6	419	13	2.65	14.9
7	367	10	1.88	16.5
8	373	11	2.92	18.9
9	325	13	3.61	21.9

[a]Incident cases (after excluding children with previous diagnoses of ODD)

[b]Weighted by screen-positive or screen-negative membership

[c]Computed by product-limit estimation using weighted annual risk

Incidence of ODD 28

Table 4

Outcome of Age of Onset on Psychopathology and Functioning (n = 461).

	Missing values	No ODD (*n* = 305)	Age onset 3-5 years-old (*n* = 113)	Age onset 6-9 years-old (*n* = 43)	3-5 vs No ODD*		6-9 vs No ODD*		6-9 vs 3-5*	
		Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	MD (95% CI)	*p*	MD (95% CI)	*p*	MD (95% CI)	*p*
SDQ- Parent										
Emotional	4	1.01 (0.88)	1.92 (1.52)	2.18 (1.42)	0.81 (0.46 ; 1.15)	**<.005**	1.01 (0.59 ; 1.44)	**<.005**	0.20 (-0.30 ; 0.71)	.430
Conduct	15	1.18 (0.84)	3.00 (1.54)	2.87 (1.32)	1.68 (1.33 ; 2.03)	**<.005**	1.44 (0.91 ; 1.98)	**<.005**	-0.24 (-0.84 ; 0.36)	.436
Hyperactivity	4	3.01 (2.08)	4.28 (2.36)	4.95 (2.33)	1.03 (0.45 ; 1.61)	**.001**	1.58 (0.80 ; 2.36)	**<.005**	0.55 (-0.35 ; 1.45)	.229
Peer	4	0.69 (0.75)	1.35 (1.24)	1.65 (1.17)	0.60 (0.33 ; 0.88)	**<.005**	0.87 (0.49 ; 1.25)	**<.005**	0.27 (-0.17 ; 0.70)	.232
Prosocial	4	1.47 (1.04)	2.14 (1.22)	1.90 (1.57)	0.58 (0.25 ; 0.90)	**.001**	0.29 (-0.29 ; 0.87)	.323	-0.29 (-0.89 ; 0.33)	.360
Total	4	5.89 (3.29)	9.90 (5.33)	11.64 (3.97)	3.45 (2.25 ; 4.65)	**<.005**	4.89 (3.62 ; 6.16)	**<.005**	1.44 (-0.21 ; 3.08)	.087
SDQ Teacher										
Emotional	2	1.28 (1.02)	1.84 (1.44)	2.14 (1.89)	0.35 (-0.01 ; 0.72)	.056	0.58 (-0.05 ; 1.21)	.073	0.23 (-0.48 ; 0.93)	.530
Conduct	14	1.22 (1.21)	2.00 (1.81)	2.25 (1.92)	0.53 (0.12 ; 0.94)	**.011**	0.61 (-0.10 ; 1.32)	.090	0.08 (-0.68 ; 0.85)	.831
Hyperactivity	2	2.86 (2.29)	3.71 (2.32)	4.39 (2.90)	0.47 (-0.10 ; 1.05)	.105	1.02 (-0.05 ; 2.10)	.062	0.55 (-0.53 ; 1.63)	.318
Peer	2	1.11 (1.01)	1.48 (1.19)	1.87 (1.36)	0.19 (-0.06 ; 0.44)	.130	0.52 (0.10 ; 0.94)	**.015**	0.33 (-0.13 ; 0.79)	.163
Prosocial	2	2.43 (1.43)	3.05 (1.78)	3.28 (2.16)	0.30 (-0.12 ; 0.72)	.166	0.43 (-0.29 ; 1.14)	.245	0.13 (-0.63 ; 0.88)	.744
Total	2	6.47 (4.26)	8.68 (5.20)	10.46 (6.40)	1.15 (-0.01 ; 2.31)	.051	2.57 (0.43 ; 4.70)	**.019**	1.42 (-0.85 ; 3.67)	.220
CGAS	0	78.33 (5.73)	66.99 (7.60)	59.03 (7.24)	-9.59 (-11.2 ; -7.94)	**<.005**	-16.64 (-19.3 ; -14.0)	**<.005**	-7.05 (-9.94 ; -4.16)	**<.005**
DSM-5		%	%	%	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
ADHD	25	15.5%	51.8%	39.3%	4.50 (2.40 ; 8.45)	**<.005**	2.43 (1.04 ; 5.68)	.041	0.54 (0.22 ; 1.30)	.170
Major depression	47	1.5%	9.4%	7.1%	5.86 (1.74 ; 19.7)	**.004**	4.35 (0.49 ; 38.9)	.188	0.74 (0.12 ; 4.65)	.751
Any Anxiety disorder	37	26.0%	57.8%	26.7%	3.43 (1.88 ; 6.25)	**<.005**	0.89 (0.33 ; 2.40)	.817	0.26 (0.09 ; 0.73)	**.011**

* Comparison between ages of first ODD diagnose are adjusted by having or not ODD treatment

In bold significant *p* values after Bonferroni correction for multiple comparison ; MD: Mean difference

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Figure 1. Design of the Study

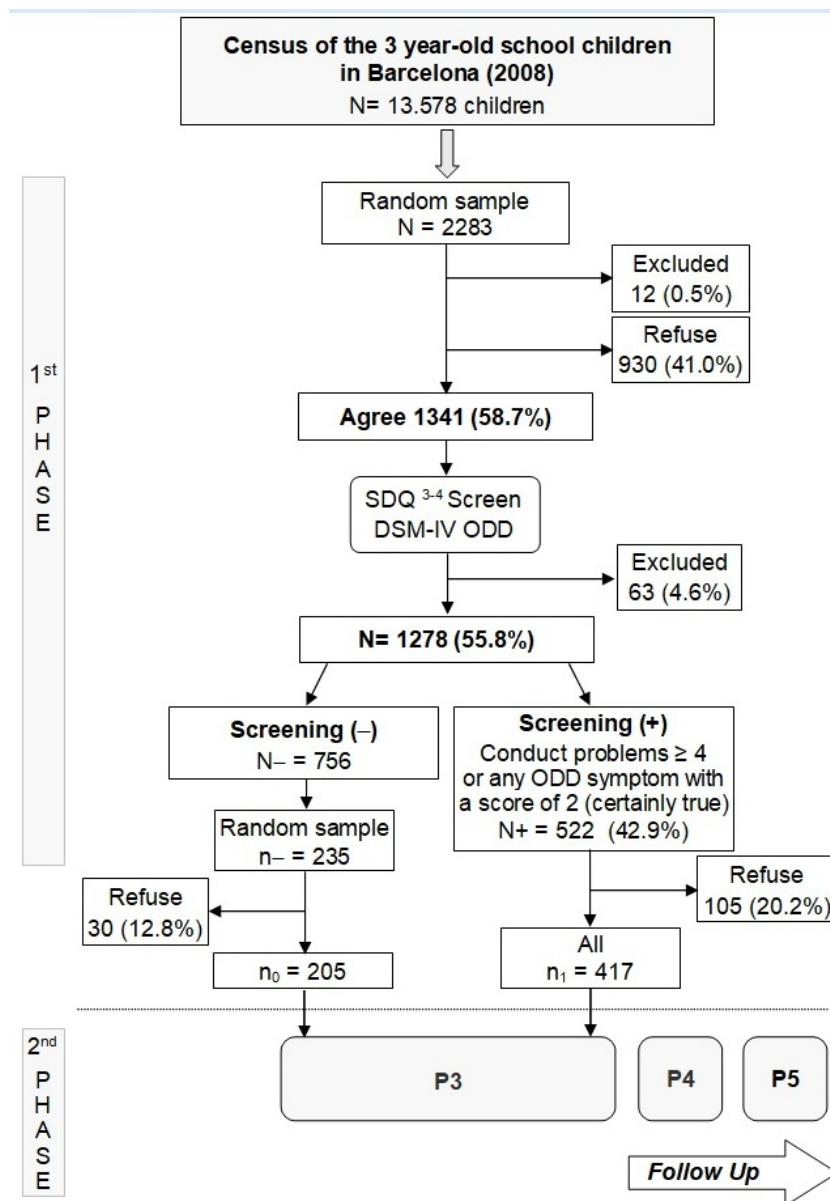**Census of the 3 year-old school children in Barcelona (2008)**
N= 13.578 children

Random sample
N = 2283

Excluded
12 (0.5%)

Refuse
930 (41.0%)

Agree 1341 (58.7%)

SDQ [3-4] Screen
DSM-IV ODD

Excluded
63 (4.6%)

N= 1278 (55.8%)

Screening (−)
N− = 756

Screening (+)
Conduct problems ≥ 4 or any ODD symptom with a score of 2 (certainly true)
N+ = 522 (42.9%)

Random sample
n− = 235

Refuse
105 (20.2%)

Refuse
30 (12.8%)

$n_0 = 205$

All
$n_1 = 417$

1st PHASE

2nd PHASE

P3

P4

P5

Follow Up

Figure 1. Desing of the study

134x194mm (120 x 120 DPI)

Table 1 online

Predictors of incident cases (n = 539)

	Age	HR*	*p*	95% CI	Harrell's C
ODD Subthreshold		6.27	**<.001**	3.85 ; 10.21	.70
ODD Irritability		1.56	**.007**	1.13 ; 2.12	.76
ODD Headstrong		2.33	**<.001**	1.84 ; 2.96	
Comorbidity (DSM5)		2.21	**.001**	1.39 ; 3.53	.58
DSM-5					
ADHD		2.64	**.002**	1.42 ; 4.93	.53
Any Anxiety		1.01	.982	0.40 ; 2.54	
Children's Behavior Questionnaire					
Negative affectivity	3	3.73	**<.001**	2.21 ; 6.29	
	4	3.06	**<.001**	2.01 ; 4.64	
	5	2.50	**<.001**	1.80 ; 3.49	
	6	2.05	**<.001**	1.55 ; 2.71	.69
	7	1.68	**<.001**	1.27 ; 2.23	
	8	1.38	.061	0.99 ; 1.93	
Effortful Control		0.88	.457	0.64 ; 1.22	
BRIEF ISCI		1.04	**<.001**	1.02 ; 1.07	.61
Alabama Parenting Questionnaire					
Positive parenting		1.01	.695	0.96 ; 1.07	
Inconsistency		1.00	.997	0.94 ; 1.07	.62
Punitive parenting		1.22	**.001**	1.08 ; 1.38	
Adult Self-Report (mother)					
Internalizing		1.06	**.002**	1.02 ; 1.10	.63
Externalizing		0.99	.991	0.94 ; 1.05	

*Weighted by screen-positive or screen-negative membership and adjusted by sex and socioeconomic status;

HR: Hazard ratio; CI: Confidence interval; BRIEF ISCI: BRIEF Inhibit and Emotional Control

In bold *p*-values < .05.

Risk factors of a first ODD diagnose from 3 to 9 years old

Table 1 online presents the hazard ratio (HR) for each risk factor with the 95%

confidence interval, its *p* value and Harrell's C for each model.

First, the variables related to ODD symptomatology were studied to know how pre-

morbid forms of ODD are related to first-incidence. The hazard of having an ODD diagnosis

was multiplied by 6.27 (95% CI=3.85 to 10.21) if there was subthreshold ODD at any of the

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follow-ups. In the same line, higher scores in the ODD dimensions of irritability and headstrong increased the risk of the incidence of ODD, each point of the dimension scores multiplying this risk by 1.56 (95% CI=1.13 to 2.12) for irritability and 2.33 (95% CI=1.84 to 2.96) for headstrong. These models obtained a moderate to good level of adequacy for the predictions (Harrell's C=.70 and .76).

Second, we studied how other psychopathologies predicted the risk of a first ODD diagnosis. The presence of comorbidity (HR=2.21, 95% CI=1.39 to 3.53), and specifically of ADHD (HR=2.64, 95% CI=1.42 to 4.93), significantly increased the risk of new cases of ODD. These models obtained a poor level of adequacy for the predictions (C=.58 and .53).

Third, the individual characteristics of the child, such as temperament and executive functioning, were studied as risk factors for the appearance of ODD. As the effect of CBQ negative affect did not meet the proportional hazard assumption, a HR was obtained for each year. The hazard of ODD increased with higher negative affectivity scores and this effect was significant and descending from ages 3 to 7 (HR=3.73, 95% CI=2.21 to 6.29 at age 3; to HR=1.68, 95% CI=1.27 to 2.23 at age 7) and not significant thereafter. For effortful control, the proportionality assumption was met, but there was no significant association with ODD. Difficulties in executive functioning in the areas of inhibition and emotional control (ISCI) were associated with risk of ODD (HR=1.04, 95% CI=1.02 to 1.07). The accuracy of the predictions was moderate-poor for these models (C=.69 and .61).

Last, we studied the influence of environmental variables. Higher scores in punitive parenting (HR=1.22, 95% CI=1.08 to 1.38) and mother's internalizing problems (HR=1.06, 95% CI=1.02 to 1.10) increased the risk of ODD. The adequacy of the predictions was poor for both models (C=.62 and .61).

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page/Line
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P. 1, L2 P. 3, L. 2-3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P. 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P. 4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	P. 6, 1st paragraph
Methods			
Study design	4	Present key elements of study design early in the paper	P. 6-7, Participants section
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P. 6-7, Participants section P. 9, Procedure Figure 1
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	P. 6-7, Participants section
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P. 7-9, Measures section P. 9-11, Statistical analysis section
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P. 7-9, Measures section
Bias	9	Describe any efforts to address potential sources of bias	P. 9, ("Interviewers were trained and were blind to the screening group") P. 10, Statistical analysis ("…adjusting estimates by sex and SES") ("Treatment for ODD at any time was introduced as covariate to adjust it confounding effect") P. 7, ("…children randomly selected")
Study size	10	Explain how the study size was arrived at	p.6 Participants
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P. 10, Statistical analysis section ("…for raw scores of quantitative outcomes")
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P. 9-11, Statistical Analysis section

		(*b*) Describe any methods used to examine subgroups and interactions	P. 9-11, Statistical Analysis section
		(*c*) Explain how missing data were addressed	P. 10, Statistical Analysis section
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P. 6-7, Participants section
		(b) Give reasons for non-participation at each stage	P. 7, 1st paragraph
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P. 6-7, Participants section and Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 4
		(c) Summarise follow-up time (eg, average and total amount)	Table 3
Outcome data	15*	Report numbers of outcome events or summary measures over time	Table 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 4 Table 1 online
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 13, paragraphs 1, 2 and 3
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 3, Strengths and limitations of the study section Page 15, 2on paragraph
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 15, 3rd paragraph
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 16, last sentence
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 17, last paragraph

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*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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First-Incidence, Age of Onset Outcomes and Risk Factors of Onset of DSM-5 Oppositional Defiant Disorder: A cohort study of Spanish children from ages 3 to 9

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Running Head: INCIDENCE OF ODD

First-Incidence, Age of Onset Outcomes and Risk Factors of Onset of DSM-5

Oppositional Defiant Disorder: A cohort study of Spanish children from ages 3 to 9

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KEYWORDS: childhood; incidence; oppositional defiant disorder; preschool; risk factors.

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ABSTRACT

Objective To examine the one-year first-incidence and prevalence of oppositional defiant disorder (ODD), the outcomes on psychopathology and functioning by age of onset and the risk factors of onset of ODD from ages 3 to 9 in children from the Spanish general population.

Design Longitudinal with 7 follow-ups and double cohort (ODD and non-ODD children).

Setting General population of preschool and elementary school children in Barcelona (Spain).

Participants On a first phase the parent-rated Strengths and Difficulties Questionnaire conduct problems scale plus oppositional defiant disorder DSM-IV symptoms were used to screen for behavioral problems. The second phase sample size contained 622 cases at age 3 and at age 9 418 remained in the study.

Results The probability of the onset of ODD showed increasing values at ages 4 (R =2.7%) and 5 years (R=4.4%). These values decreased until age 7 (R=1.9%) and increased again until age 9 (R=3.6%). Up to 9 years old the cumulative risk of new cases of ODD was 21.9%. Early onset was associated with a higher risk of depression comorbidity and later onset with higher functional impairment and symptomatology. Subthreshold ODD, high scores in irritability and headstrong dimensions, ADHD and other comorbidity, negative affectivity until age 7, difficulties in inhibit and emotional control, punitive parenting and maternal internalizing problems were risk factors of a first episode of ODD during this seven-year period.

Conclusions The risk of new cases of ODD in the general population at preschool age and during childhood is high. Preschool age is a target period for preventive interventions. Identified risk factors are objectives for targeted and indicated interventions.

Strengths and limitations of the study

Strengths:

- The length of the follow-up period (7 years) including two different developmental stages, preschool and childhood.

- The information on risk factors and outcomes obtained from parents and teachers.

- The consideration of risk factors in Cox regression models as time dependent covariates instead of fixed covariates.

Limitations:

- The lower participation of low SES families and the non-random attrition for some outcomes may have led to bias in the estimates.

- The low incidence of ODD made necessary to cluster ages (3-5 and 6-9) for the analysis of the influence of ODD age of onset on psychopathology and functioning.

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FIRST-INCIDENCE, AGE OF ONSET OUTCOMES AND RISK FACTORS OF ONSET OF DSM-5 OPPOSITIONAL DEFIANT DISORDER: A COHORT STUDY OF SPANISH CHILDREN FROM AGES 3 TO 9

According to epidemiological studies the proportion of children and adolescents with mental health problems is 13.4%(1). These disorders are stable and continue into later life with adverse adults outcomes(2). Therefore, childhood is a target period for the early identification and prevention of mental disorders.

Oppositional defiant disorder (ODD), a pattern of negativistic, defiant, disobedient and hostile behaviour, is one of the most prevalent disorders from preschool age to adulthood(3, 4). The pooled prevalence is 3.6% up to age 18(1). ODD is accompanied by various concurrent disorders (attention deficit/hyperactivity disorder-ADHD), successive comorbidity (conduct disorder, anxiety, depression, substance use)(5, 6) and functional impairment(7, 8). Symptomatology is stable and sufferers have difficulties in the transition to adulthood(9). The amount of children and families affected and the severe consequences that compromise healthy mental development underscore the need to know when the first onset occurs and the factors that predict this onset in order to plan appropriate preventive strategies.

Currently, we know how many children in the population are affected by ODD at a given point in time; that is, the prevalence, a measure of the status of the disease. We do not know, however, how many new cases appear at different developmental stages; that is, incidence, a measure of newly occurring cases of the disease during a specific developmental period(10). Because there is often a low number of incident cases, incidence studies require cohort designs with large size samples. Literature shows that there is a dearth of studies about the incidence of psychiatric disorders in childhood and adolescence. The available data on ODD mostly focus on adolescents and youths. Roberts(11) reported that the risk of new cases of ODD for adolescents in a 12-month period was 1.56% and Benjet(12) found a 5% 8-year

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incidence for 19- to 26-year-old youth. There are no studies on the incidence of ODD during preschool and childhood. Neither do we know the differential consequences of the disorder according to age of onset. Literature on general mental disorders has reported that early onset is associated with greater severity, persistence and lack of response to treatment(13). Age of onset is an important data to advise on mental health policies(14).

Several risk factors have been reported in the literature on ODD. Child risk factors include genetic influences(15), difficult temperament(16), difficulties in processing social information(17), sex(18) and ADHD(19). The contextual factors reported include socioeconomic status, parenting practices, parental psychopathology, family conflict and poor attachment(15, 20). Incidence figures, which report on new cases of disease, are more useful for identifying risk factors than prevalence studies, which include both chronic and new cases(21). No previous studies have examined the risk factors of ODD by considering new cases. Only Roberts(11) adopted this approach in adolescents, reporting that a younger age, poor family satisfaction, passive coping and low mastery, school and economic stress and poor relations with parents were predictors of incident cases of ODD.

Furthermore, ODD is a continuous disorder that starts early in life and persists into adulthood(9). It is therefore imperative to know for prevention purposes how the early manifestations of ODD symptomatology affect the definite appearance of the full disorder. Several dimensions of ODD have been identified to explain its underlying structure: irritable (including loses temper, angry and touchy); headstrong (argues, defies, annoys, blames) and hurtful (spiteful-vindictive)(22). Rowe(20) showed how ODD dimensions predict full ODD diagnosis. Moreover, the literature has shown that subthreshold conditions are risk factors for developing similar (homotypic) or different (heterotypic) full-syndrome(23) and that they constitute a major public mental health burden(24).

The objective was to study annually the proportion of incident cases of ODD from ages 3 to 9 (preschool through childhood), to ascertain the differential outcomes by age of onset and to test if previously reported risk factors associated with ODD are prospective risk factors of incident cases at these developmental stages.

METHOD

Participants

The initial sample consisted of 2,283 children randomly selected from early childhood schools in Barcelona (Spain)(25). A two-phase design was employed. In the first-phase of sampling, 1,341 families (58.7%) agreed to participate (33.6% high socioeconomic status (SES), 43.1% middle and 23.3% low; 50.9% boys). To ensure that children with possible behavioral problems participated, the parent-rated Strengths and Difficulties Questionnaire (SDQ[3-4]) conduct problems scale(26) plus ODD DSM-IV symptoms were used to screen. Two groups were considered: screen-positive (all children with SDQ scores ≥4, percentile 90, or with a positive response to any of the eight DSM-IV ODD symptoms) and screen-negative (a random group comprising 28% of children who did not reach the positive threshold). The sample size was determined for detecting OR ≥ 1.8 between psychopathology and risk factors, using a test of hypothesis for risk α = .05 and power of .80. As the planned follow-up was 12 years long, the sample size was increased 50% for losses.

The final sample for the follow-ups (second-phase) included 622 children (Figure 1) comprising all the children from the screen-positive group whose families accepted to participate (N = 417; 49.4% boys) and a random sample from the screen-negative group (N = 205; 51.2% boys). To select participants from screen-negative group children of each classroom were alphabetically numbered without including the name of the child nor the school. Then they were randomly permutated using SPSS random number generator, and the

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first 30% was selected. The percentage of drop-outs at annual follow-up from ages 4 to 9 was

similar in the two screen groups (χ^2 = 0.72, p = .798 at age 4; χ^2 = 0.31, p = .575 at age 5; χ^2

= 1.36, p = .244 at age 6; χ^2 = 0.02, p = .877 at age 7; χ^2 = 0.49 and p = .484 at age 8; χ^2 =

0.20 and p = .652 at age 9). No differences in sex (χ^2 =0.07; p =.793) or type of school (χ^2

=0.72; p =.396) were found on comparing completers and drop-outs during the seven years of

annual follow-ups. However, the SES of those leaving the study until age 9 was lower (χ^2

=20.89; p <.001). Finally, to assess randomness of attrition the outcome scores at age 3

between cases and drop-outs at age 9 were compared. For 6 out of the 16 outcomes, scores at

age 3 were higher for drop-outs than for completers at age 9.

From the initial 622 children, 65 who presented an ODD diagnosis at the start of the

study (age 3) and 18 who left the study at the second follow-up (age 4) were excluded for the

analysis of risk factors because lack of information (N =539). Decrements in sample size at

successive follow-ups were either due to attrition or to the exclusion of children who had

already presented a first ODD diagnosis. Demographic characteristics are shown in Table 1.

Measures

Diagnostic Interview of Children and Adolescents for Parents of Preschool Children (DICA-

PPC)

The DICA-PPC(27) is a computerised semi-structured interview which generates diagnoses

through algorithms following DSM-5. The diagnosis of ODD was obtained annually. The

interviews in the first assessment gathered data from the first 3 years of life. ADHD, major

depression, any anxiety disorders (separation, generalized, social anxiety or specific phobias)

and comorbidity (ADHD, conduct disorder, major depression or any anxiety plus ODD) were

obtained at each age from 3 to 9 years old. Subthreshold ODD was defined as cases that did

not meet the threshold criteria of four symptoms for the diagnosis but presented impairment

or distress. Rowe's(20) ODD dimensions were used (*irritable* and *headstrong)*. Inter-interviewer agreement in the diagnoses ranged from Kappa coefficients from .83 to 1 (mean kappa .92; being .84 for ODD), indicating a good to excellent agreement between interviewers.

The *Strengths and Difficulties Questionnaire* (SDQ)(26) assesses emotional and behavioural problems with 25 items with 3 response options organized in 5 scales. It was answered by the parents and teachers. Cronbach's alpha for parents range from .55 (conduct) to .85 (hyperactivity) and for teachers from .69 (conduct) to .88 (total).

The *Children's Global Assessment Scale* (CGAS)(28) is a global measure of functional impairment rated by the interviewer. Scale scores range from one (maximum impairment) to 100 (normal functioning). Scores above 70 indicate normal adaptation.

Children's Behavior Questionnaire Short Form and Very Short Form(29) measure reactive and self-regulative temperament with 94 and 36 items respectively on a 7-point Likert-type scale. These were answered by the parents when the children were 3, 4 and 5 years old (short form) and 7 years old (very short form). The broad dimensions negative affectivity and effortful control were considered. Cronbach's alpha in the sample ranged from .71 for effortful control at age 7 to .85 for negative affectivity at age 5.

The *Behavior Rating Inventory of Executive Function preschool version* (BRIEF-P)(30), answered by teachers when children were 3 years old, assesses behaviors reflecting the executive functions in daily life. The broad dimension that combine inhibit (control of

impulses and behavior) and emotional control (appropriate modulation of emotional responses) (ISCI) was used (Cronbach's alpha: .94).

The *Alabama Parenting Questionnaire-Preschool* (APQ-Pr)(31), measures parental practices in three dimensions (24 items): positive discipline techniques, inconsistent parenting and punitive parenting(32). They were obtained at ages 3 and 6. Cronbach's alpha for the three dimensions was .75, .62 and .42 at age 3, and .74, .66 and .52 at age 6, respectively.

The *Adult Self-Report* (ASR)(33) assesses dimensional psychopathology (126 itemsI in adults. The mothers answered the questionnaire when the children were 3 and 8 years old. Internalizing and externalizing scale scores were analyzed (Cronbach's alpha .85 and .80 respectively at the last follow-up).

Patient and Public Involvement statement

Oppositional defiant disorder is a social problem and families and schools complain about how to manage disruptive behavior disorders at home and at the school. We wanted to investigate about the development of this problem to know the best developmental moments and their risk factors to help the families and the teachers to prevent oppositionality. Families and schools were freely and actively involved in the study. Families and schools were informed yearly of the results of the previous follow-up and were oriented about what to do to improve the behavior when necessary. Every 3 years they received a written report about the evolution and development of the child. Teachers received a 15 hours course about *How to manage disruptive behavior disorder at the school-room* at the beginning of different school levels (preschool -age 3-, elementary -ages 6 and 9).

Procedure

The project was approved by the Ethics Committee for Human and Animal Experimentation of the Universitat Autònoma de Barcelona. Families were recruited at the schools and gave written consent. The families who agreed to participate and met the screening criteria were contacted each year and interviewed at the school. Interviewers were trained and were blind to the screening group. All the interviews were audio-recorded and supervised. The data was collected between November-2009 and July-2016.

Statistical Analysis

The data was analyzed with Stata 15 for Windows. Since all the data were collected using a double-phase screening design, all analyses were weighted by assigning each child a value that was inverse to the probability of random selection in the second phase of sampling. Cases with missing data were excluded separately for each analysis (pairwise deletion). The incidence proportion was calculated for one-year time periods beginning at 4 years old by dividing the number of new cases of first ODD diagnosis (incident cases) by the number of children at risk, i.e. the number of cases at the beginning of the period excluding those who had previous diagnoses of ODD. This ratio is also called Risk (R) and it estimates the 'probability of an event during a specified period of time'(10). Cumulative risk estimates the risk of ODD from 0 years old to each time period; because of the lost cases across the study, cumulative risk was computed by the Kaplan-Meier product-limit estimation(34) using the weighted annual risk.

The analysis of differences in psychopathology and functioning by age of onset of ODD was made by ANOVA for raw scores of quantitative outcomes and logistic regression for binary outcomes. Age of onset was grouped into preschool (3-5) and school (6-9) periods. The group without ODD was also considered and post-hoc comparisons corrected by

Bonferroni for multiple comparisons were estimated. Treatment for ODD at any time, current

ODD diagnosis and number of years with an ODD diagnosis were introduced as covariates to

adjust for confounding effects.

To analyze the predictors of the risk of an ODD diagnosis, several Cox proportional

hazard regression models were estimated, grouping predictors (risk factors) by the

measurement instrument and adjusting estimates by sex and SES. Predictors were considered

as time dependent between ages 3 to 8 to benefit from the most recent available information.

As a consequence and because of the multiple-record structure of the data matrix (each child

had one data record for each follow-up period), the robust variance estimator(35) was used.

No competitive events were considered due to the high specificity of an ODD diagnosis and

to the characteristics of the sample, with neither deaths nor physical comorbidities that

prevented an ODD diagnosis. Proportional hazard assumption was verified by calculating the

significance value of the interaction between predictors and time. In the presence of

significant interaction, the hazard ratio (HR) for the involved predictor was obtained

separately for each year of follow-up, corresponding to ages 3 to 8. For each Cox regression

model, Harrell's *C* index(36) was calculated to evaluate the adequacy of the predictions

(values ≥ .70 are considered good).

RESULTS

Prevalence of ODD from 3 to 9 years old

Table 2 presents the number of children in the study, the number of ODD diagnoses

and the prevalence for each age. Prevalence oscillated between 6.0% (age 3) and 8.8% (age

9).

First-Incidence and cumulative risk of ODD from 4 to 9 years old

The first three columns in Table 3 show the cases at risk (without an ODD diagnosis) at the beginning of each year period, the number of new cases diagnosed with ODD during that year and the incidence. The probability of the appearance of ODD showed a cubic shape, with risk increasing from age 4 to age 5 (R=2.7% to 4.4%), followed by a decrease until age 7 (R=1.9%) and a new increase at ages 8 and 9 (R=2.9%, 3.6%). The last column in Table 3 shows the cumulative risk of having a first ODD diagnosis up to 9 years old, which reached 21.9%. Figure 2 shows prevalence of ODD and incidence of first ODD diagnosis by age .

Outcomes of age of onset of ODD

Table 4 shows the scores and percentages of psychopathology and functioning for children with onset of ODD at 3-5 and 6-9 years old and for those without ODD, as well as the multiple comparisons between the three groups with the mean difference (MD) or the odds ratio (OR) and their 95% confidence intervals. Controlling by current ODD diagnosis, the number of years of duration of ODD and treatment received, children with onset at 3-5 years old scored lower on functional impairment, which indicates worse functioning (MD = -7.17), and presented higher comorbidity with major depression (OR = 5.76) in comparison to children without ODD. Children with onset of ODD at 6-9 years old scored higher on all the scales of parent's SDQ except prosocial (MD between 0.63 for conduct and 1.68 for hyperactivity) and on total (MD = 3.95), and presented worse functioning (MD = -13.06) in comparison with children without ODD. There were differences in the total SDQ score (MD = 2.99) and in peer problems (MD = 0.66) between preschooler and late ODD onset, the latter showing higher scores. Moreover, children with onset of ODD at 6-9 years old presented higher functional impairment than those with onset at 3-5 years old (MD = -5.89).

Risk factors of incident ODD diagnose from 3 to 9 years old

Hazard ratio (HR) for each risk factor with the 95% confidence interval, its *p* value

and Harrell's *C* for each model were calculated (See Supplementary Table 1). The hazard of

having an ODD diagnosis was increased by subthreshold ODD symptomatology (HR=6. 27,

95% CI 3.85 to 10.21), high scores on ODD dimensions of irritability (HR=1.56, 95% CI 1.13

to 2.12) and headstrong (HR=2.33, 95% CI 1.84 to 2.96), comorbidity (HR=2.21, 95% CI

1.13 to 3.53), specifically of ADHD (HR=2.64, 95% CI 1.42 to 4.93), higher negative

affectivity (HR=3.73, 95% CI 2.21 to 6.29 at age 3 to HR=1.68, 95% CI 1.27 to 2.23 at age

7), difficulties in inhibition and emotional control (HR=1.04, 95% CI 1.02 to 1.07), higher

scores in punitive parenting (HR=1.22, 95% CI 1.08 to 1.38) and mother's internalizing

problems (HR=1.06, 95% CI 1.02 to 1.10).

The capability to predict new ODD first-incident cases from the subsets of risk factors

was low in general. Only the first model with "being an ODD substreshold" as predictor, and

the second model with "ODD Irritability and Headstrong" scores as predictors showed

Harrell's *C* ≥ .70.

DISCUSSION

To our knowledge this is the first study reporting on not only the one-year incidence of

ODD in a seven-year follow-up design covering ages 3 to 9 and the effects of different age

ranges of onset, but also their risk factors and the DSM-5 prevalence. We found that the

probability of the appearance of ODD shows a cubic shape with higher values for the

preschool period, a decrease at the start of childhood (ages 6 and 7) and another increase

when approaching puberty (ages 8 and 9). Prevalence was around 6-7% between ages 3 and 8,

increasing to 8.8% by age 9. An early onset of ODD is more closely associated with the

presence of depressive comorbidity, but the functional impairment of those with later onset is

most marked and their parents report higher symptomatology. Risk factors of incidence were

identified.

Throughout development prevalence was high and very stable (6-7%), with the highest

value at 9 years old. These percentages indicate the need to allocate resources such as services

and training to the parents, teachers and professionals involved with the children in these age

ranges that have already developed the disorder.

2.7 and 4.4 out of 100 preschoolers aged 4 and 5, respectively, and between 1.9 and

3.6 out of 100 children aged 6 to 9 will develop a first episode of ODD in one year. It is

remarkable that at the end of the follow-ups the cumulative risk was high, indicating that up

to 9 years old the risk of presenting ODD is 21.9%. This risk is highest in the preschool

period, which cumulates 12.6% of the risk, the remaining 9.3% occurring in childhood. These

values are noteworthy in terms of public mental health indicators if one considers the short-

term impact ODD has on the lives of children, families, teachers and schools(8), as well as the

long-term effects until adulthood(9). Specifically, these results point to the need to pay

attention to the preschool period if the goal is to prevent ODD. On the one hand, preschool

age is when the child is acquiring important skills related to ODD, such as self-regulation and

executive functioning, and when parents adjust their parenting practices(37). It is important to

intervene in this period when the early signs of dysfunction become apparent. On the other

hand, programmes that have been shown to effectively treat ODD(38-40) and prevent it(41,

42) are currently available.

An early age of onset has typically been associated with worse mental health

outcomes(13). This is also true for ODD regarding comorbidity. Specifically, the risk of

depression in children who debut ODD at preschool age multiplies by 5.76 compared to

children without ODD. Comparing early versus later onset after strict control by confounding

variables, later onset increases the risk of higher symptomatology (general and in peer

problems) and difficulties in functioning. One of the contributions of studying age of onset is to have available information for targeting prevention that focuses on early intervention in incipient mental disorders and on primary prevention of secondary disorders(13). Thus, our results once again suggest the need to intervene at early ages. This implication is also supported by the finding that for those starting later (ages 6-9), the impairment in functioning and in symptomatology is more severe. Therefore, paying attention to prodromal indicators and risk factors to prevent the full development of ODD is crucial.

Regarding risk factors, our goal was to confirm the risk of first onset of ODD using some of the main risk factors reported previously in the literature. No previous studies have been carried out with incident cases. The strength of the association for some of the predictors is remarkable. We found that pre-morbid forms of ODD (subthreshold, high scores in the ODD dimensions irritability and headstrong) were the strongest predictor of onset of full ODD. Identifying pre-morbid cases is of great value for the indicated prevention of ODD, given that the group at risk presents objective markers (ODD symptoms). Similarly, children with other psychopathology, and specifically ADHD, and individual characteristics, such as difficulties in inhibit-emotional control are also at risk of onset of ODD. Also, our results indicate that difficulties regulating negative emotions are at a higher risk of ODD onset, especially from very early ages, while the risk diminishes with age. Last, unsupportive environments, such as punitive parenting practices and maternal internalizing problems, predicted the emergence of an ODD diagnosis, which is also in line with previous literature(15, 43). Predictive capability assessed by Harrell's *C* was generally low to moderate, indicating that to predict first-incident ODD cases other predictors are needed in addition to the clinical risk factor considered. However, it is necessary to consider the low number of predictors included in each model.

Strengths of the study are that the diagnostic information was obtained via semi-structured interviews based on DSM-5 criteria, the length of the follow-up period (7 years), the inclusion of two different developmental stages, preschool and childhood, and the fact that the estimates of incidence were not overestimated, given that previous diagnoses until age 3 were also made. Age of onset studies have been carried out mostly through retrospective design, which is a limitation. We studied age of onset through a prospective design. Furthermore, the information on risk factors was obtained from parents and teachers. However, some limitations must be considered when interpreting the results. The diagnostic information, based on data from just one source, the parents, and the lower participation of low SES families may have led to bias in the estimates. A second limitation refers to the non-randomness of attrition in 6 out of the 16 outcomes analysed as risk factors of first ODD diagnose. However, as shown in several populations, attrition is associated with adverse psychosocial variables and high levels of psychological distress (44, 45). Also, some of the scales of the APQ-Pr presented low internal consistency and the results should thus be interpreted with caution. Finally, the fact that increasing the age of the children the number of incident cases diminished, limited the statistical power.

Synthesizing, oppositional defiant disorder is one of the most prevalent disorders in our society. It has important consequences in the development of the child and in the functioning of the family. It starts very early in life but we do not know how many new cases appear every year, nor the consequences it has depending on the age of onset. Our study reports that the probability of appearance of oppositional defiant disorders is highest by age 5 and, afterwards, by age 9, when approaching to puberty. Most of the new cases of oppositional disorder appeared in preschool age (12.6%). By age 9 there is a cumulative risk of new onset of 21.9%. Early onset at preschool age is associated with comorbidity with anxiety and depression; childhood onset is associated with higher functional impairment.

These results indicate the burden of oppositional disorder for public health and point to the

need of focusing in preschool age for preventive purposes. To allocate resources in this

developmental period and paying attention to prodromal indicators and risk factors to prevent

the full development of ODD is crucial. Our results are generalizable to Spanish children

mostly from mean and high-mean socioeconomic levels until age 9.

Contributorship statement

LE designed the study and wrote the paper with JBN. JBN analyzed data. JMD contributed to

data analysis. N. de la O and EP collaborated in the writing editing of the manuscript. All the

authors contributed reviewing the final version of the manuscript.

Availability of data and materials

Data cannot be publicly available due to ethical restrictions protecting the confidentiality of

the families involved. Data are available to interested researchers after signing a consent of

confidentiality form as the authors had previously signed to obtain the data from the families

of the sample. Researchers must be working in clinical child psychology in a public funded

project. To request the anonymous data, please contact the corresponding author.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical

standards of the relevant national and institutional committees on human experimentation and

with the Helsinki Declaration of 1975, as revised in 2008.

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Conflict of interests

The authors have no conflicts of interests.

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Table 1

Demographic Characteristics of the Sample at age 3 (N = 622)

Age (mean; *SD*)	3.8 (.33)
Sex; *n (%)*	
Male	311 (50.0)
Race/ethnicity; *n (%)*	
Non-Hispanic White	557 (89.5)
Hispanic-American	46 (7.4)
Other	19 (3.1)
SES; n *(%)*	
High	205 (33.0)
Middle	280 (45.0)
Low	137 (22.0)

Table 2

DSM-5 ODD Prevalence from 3 to 9 years-old.

Age (years-old)	Total cases	ODD cases	Prevalence* %
3	622	65	6.03
4	604	63	7.08
5	535	46	7.09
6	509	47	7.04
7	456	41	6.99
8	469	35	6.09
9	418	40	8.83

*Weighted by screen-positive or screen-negative membership: number of children with ODD divided by the total sample size at that age.

Table 3

ODD One-Year First-Incidence and Cumulative Risk from 0 to 9 years-old.

Age (years-old)	Cases at risk	Incident ODD cases[a]	First ODD diagnosis	
			Risk[b] %	Cumulative Risk[c] (%)
0 to 3				6.0
4	541	23	2.71	8.6
5	463	20	4.39	12.6
6	419	13	2.65	14.9
7	367	10	1.88	16.5
8	373	11	2.92	18.9
9	325	13	3.61	21.9

[a]Incident cases (after excluding children with previous diagnoses of ODD)

[b]Weighted by screen-positive or screen-negative membership

[c]Computed by Kaplan-Meier product-limit estimation using weighted annual risk

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Table 4

Outcome of Age of Onset on Psychopathology and Functioning (n = 461).

	Missing values	No ODD (*n* = 305)	Age onset 3-5 years-old (*n* = 113)	Age onset 6-9 years-old (*n* = 43)	3-5 vs No ODD*		6-9 vs No ODD*		6-9 vs 3-5*	
		Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	MD (95% CI)	*p*	MD (95% CI)	*p*	MD (95% CI)	*p*
SDQ-Parent										
Emotional	4	1.01 (0.88)	1.92 (1.52)	2.18 (1.42)	0.29 (-0.35 ; 0.92)	.379	0.82 (0.27 ; 1.36)	**.003**	0.53 (-0.16 ; 1.22)	.133
Conduct	15	1.18 (0.84)	3.00 (1.54)	2.87 (1.32)	0.42 (0.02 ; 0.82)	.040	0.63 (0.18 ; 1.08)	**.006**	0.22 (-0.24 ; 0.67)	.353
Hyperactivity	4	3.01 (2.08)	4.28 (2.36)	4.95 (2.33)	0.65 (-0.28 ; 1.57)	.171	1.68 (0.78 ; 2.57)	**<.005**	1.03 (-0.01 ; 2.07)	.052
Peer	4	0.69 (0.75)	1.35 (1.24)	1.65 (1.17)	0.09 (-0.33 ; 0.51)	.679	0.75 (0.25 ; 1.25)	**.004**	0.66 (0.07 ; 1.25)	**.027**
Prosocial	4	1.47 (1.04)	2.14 (1.22)	1.90 (1.57)	0.30 (-0.32 ; 0.91)	.340	0.17 (-0.40 ; 0.73)	.560	-0.13 (-0.85 ; 0.59)	.719
Total	4	5.89 (3.29)	9.90 (5.33)	11.64 (3.97)	0.97 (-0.81 ; 2.75)	.286	3.95 (2.47 ; 5.44)	**<.001**	2.99 (1.20 ; 4.77)	**.001**
SDQ-Teacher										
Emotional	2	1.28 (1.02)	1.84 (1.44)	2.14 (1.89)	0.47 (-0.25 ; 1.18)	.201	0.61 (-0.23 ; 1.44)	.153	0.14 (-0.78 ; 1.06)	.762
Conduct	14	1.22 (1.21)	2.00 (1.81)	2.25 (1.92)	0.16 (-0.41 ; 0.72)	.587	0.37 (-0.40 ; 1.14)	.347	0.21 (-0.60 ; 1.02)	.604
Hyperactivity	2	2.86 (2.29)	3.71 (2.32)	4.39 (2.90)	0.18 (-0.82 ; 1.17)	.730	1.22 (-0.16 ; 2.60)	.082	1.05 (-0.40 ; 2.49)	.157
Peer	2	1.11 (1.01)	1.48 (1.19)	1.87 (1.36)	0.05 (-0.36 ; 0.47)	.799	0.50 (0.02 ; 0.97)	.041	0.44 (-0.05 ; 0.94)	.080
Prosocial	2	2.43 (1.43)	3.05 (1.78)	3.28 (2.16)	-0.25 (-0.84 ; 0.34)	.400	0.09 (-0.74 ; 0.92)	.835	0.34 (-0.47 ; 1.16)	.411
Total	2	6.47 (4.26)	8.68 (5.20)	10.46 (6.40)	0.35 (-1.56 ; 2.26)	.721	2.44 (-0.38 ; 5.26)	.089	2.09 (-0.84 ; 5.03)	.162
CGAS	0	78.33 (5.73)	66.99 (7.60)	59.03 (7.24)	-7.17 (-10.0 ; -4.31)	**<.001**	-13.06 (-16.1 ; -9.99)	**<.001**	-5.89 (-9.16 ; -2.62)	**<.001**
DSM-5		%	%	%	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
ADHD	25	15.5%	51.8%	39.3%	2.55 (0.93 ; 6.97)	.068	2.53 (0.91 ; 7.03)	.076	0.99 (0.34 ; 2.85)	.986
Major depression	47	1.5%	9.4%	7.1%	5.76 (1.15 ; 28.8)	**.033**	4.06 (0.56 ; 29.51)	.166	0.70 (0.11 ; 4.50)	.712
Any Anxiety disorder	37	26.0%	57.8%	26.7%	2.23 (0.91 ; 5.46)	.079	1.20 (0.40 ; 3.58)	.747	0.54 (0.16 ; 1.81)	.316

* Comparison between ages of first ODD diagnose are adjusted by: having or not ODD treatment, current ODD diagnose and number of years with an ODD diagnose

In bold significant *p* values after Bonferroni correction for multiple comparison ; MD: Mean difference
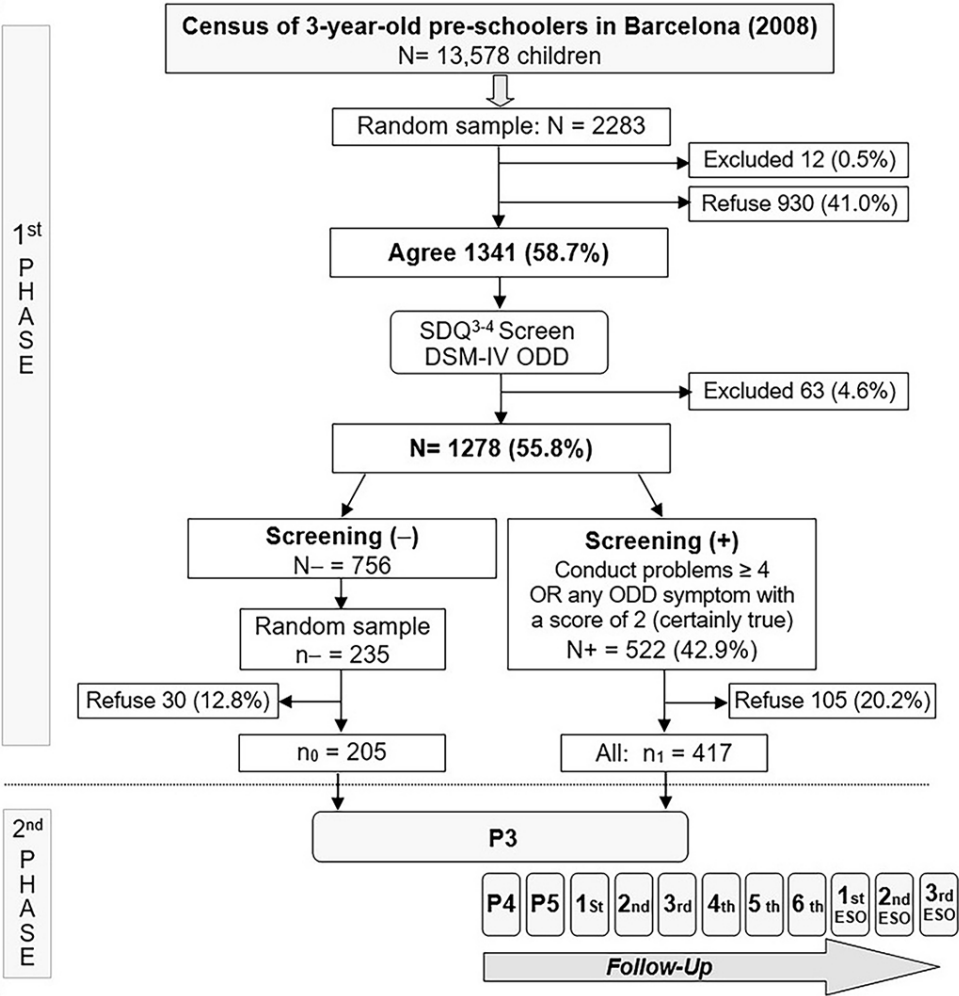
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Figure 1.

Design of the Study

Figure 2.

Prevalence and first incidence (risk) of ODD diagnose from 3 to 9 years old
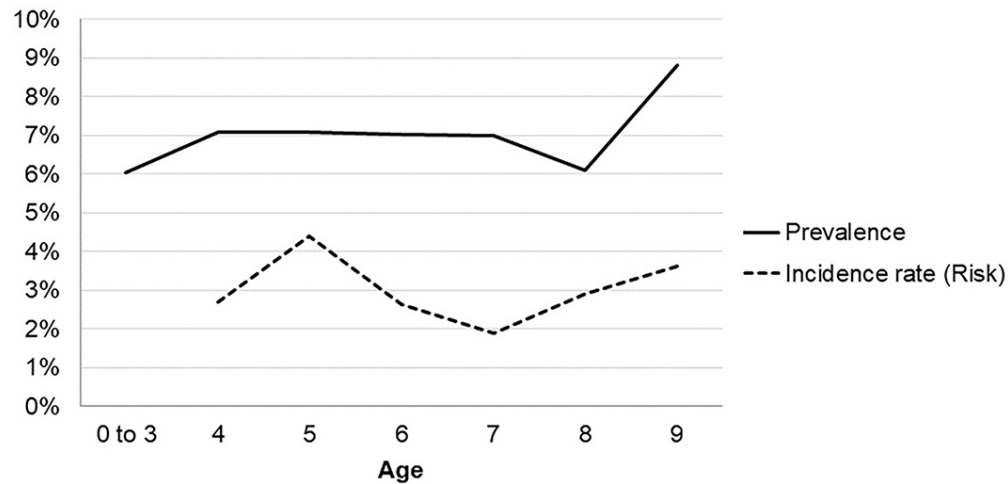
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Design of the Study

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Prevalence and first incidence (risk) of ODD diagnose from 3 to 9 years old

90x90mm (300 x 300 DPI)

Table 1 online

Predictors of incident cases (n = 539)

	Age	HR*	*p*	95% CI	Harrell's C
ODD Subthreshold		6.27	**<.001**	3.85 ; 10.21	.70
ODD Irritability		1.56	**.007**	1.13 ; 2.12	.76
ODD Headstrong		2.33	**<.001**	1.84 ; 2.96	
Comorbidity (DSM5)		2.21	**.001**	1.39 ; 3.53	.58
DSM-5					
ADHD		2.64	**.002**	1.42 ; 4.93	.53
Any Anxiety		1.01	.982	0.40 ; 2.54	
Children's Behavior Questionnaire					
Negative affectivity	3	3.73	**<.001**	2.21 ; 6.29	
	4	3.06	**<.001**	2.01 ; 4.64	
	5	2.50	**<.001**	1.80 ; 3.49	
	6	2.05	**<.001**	1.55 ; 2.71	.69
	7	1.68	**<.001**	1.27 ; 2.23	
	8	1.38	.061	0.99 ; 1.93	
Effortful Control		0.88	.457	0.64 ; 1.22	
BRIEF ISCI		1.04	**<.001**	1.02 ; 1.07	.61
Alabama Parenting Questionnaire					
Positive parenting		1.01	.695	0.96 ; 1.07	
Inconsistency		1.00	.997	0.94 ; 1.07	.62
Punitive parenting		1.22	**.001**	1.08 ; 1.38	
Adult Self-Report (mother)					
Internalizing		1.06	**.002**	1.02 ; 1.10	.63
Externalizing		0.99	.991	0.94 ; 1.05	

*Weighted by screen-positive or screen-negative membership and adjusted by sex and socioeconomic status;

HR: Hazard ratio; CI: Confidence interval; BRIEF ISCI: BRIEF Inhibit and Emotional Control

In bold *p*-values < .05.

Risk factors of a first ODD diagnose from 3 to 9 years old

Table 1 online presents the hazard ratio (HR) for each risk factor with the 95%

confidence interval, its *p* value and Harrell's C for each model.

First, the variables related to ODD symptomatology were studied to know how pre-

morbid forms of ODD are related to first-incidence. The hazard of having an ODD diagnosis

was multiplied by 6.27 (95% CI=3.85 to 10.21) if there was subthreshold ODD at any of the

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follow-ups. In the same line, higher scores in the ODD dimensions of irritability and headstrong increased the risk of the incidence of ODD, each point of the dimension scores multiplying this risk by 1.56 (95% CI=1.13 to 2.12) for irritability and 2.33 (95% CI=1.84 to 2.96) for headstrong. These models obtained a moderate to good level of adequacy for the predictions (Harrell's C=.70 and .76).

Second, we studied how other psychopathologies predicted the risk of a first ODD diagnosis. The presence of comorbidity (HR=2.21, 95% CI=1.39 to 3.53), and specifically of ADHD (HR=2.64, 95% CI=1.42 to 4.93), significantly increased the risk of new cases of ODD. These models obtained a poor level of adequacy for the predictions (C=.58 and .53).

Third, the individual characteristics of the child, such as temperament and executive functioning, were studied as risk factors for the appearance of ODD. As the effect of CBQ negative affect did not meet the proportional hazard assumption, a HR was obtained for each year. The hazard of ODD increased with higher negative affectivity scores and this effect was significant and descending from ages 3 to 7 (HR=3.73, 95% CI=2.21 to 6.29 at age 3; to HR=1.68, 95% CI=1.27 to 2.23 at age 7) and not significant thereafter. For effortful control, the proportionality assumption was met, but there was no significant association with ODD. Difficulties in executive functioning in the areas of inhibition and emotional control (ISCI) were associated with risk of ODD (HR=1.04, 95% CI=1.02 to 1.07). The accuracy of the predictions was moderate-poor for these models (C=.69 and .61).

Last, we studied the influence of environmental variables. Higher scores in punitive parenting (HR=1.22, 95% CI=1.08 to 1.38) and mother's internalizing problems (HR=1.06, 95% CI=1.02 to 1.10) increased the risk of ODD. The adequacy of the predictions was poor for both models (C=.62 and .61).

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page/Line
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P. 1, L2 P. 3, L. 2-3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P. 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P. 4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	P. 6, 1st paragraph
Methods			
Study design	4	Present key elements of study design early in the paper	P. 6-7, Participants section
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P. 6-7, Participants section P. 9, Procedure Figure 1
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	P. 6-7, Participants section
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P. 7-9, Measures section P. 9-11, Statistical analysis section
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P. 7-9, Measures section
Bias	9	Describe any efforts to address potential sources of bias	P. 9, ("Interviewers were trained and were blind to the screening group") P. 10, Statistical analysis ("…adjusting estimates by sex and SES") ("Treatment for ODD at any time was introduced as covariate to adjust it confounding effect") P. 7, ("…children randomly selected")
Study size	10	Explain how the study size was arrived at	p.6 Participants
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P. 10, Statistical analysis section ("…for raw scores of quantitative outcomes)"
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P. 9-11, Statistical Analysis section

		(b) Describe any methods used to examine subgroups and interactions	P. 9-11, Statistical Analysis section
		(c) Explain how missing data were addressed	P. 10, Statistical Analysis section
		(d) If applicable, explain how loss to follow-up was addressed	NA
		(e) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P. 6-7, Participants section
		(b) Give reasons for non-participation at each stage	P. 7, 1st paragraph
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P. 6-7, Participants section and Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 4
		(c) Summarise follow-up time (eg, average and total amount)	Table 3
Outcome data	15*	Report numbers of outcome events or summary measures over time	Table 3
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 4 Table 1 online
		(b) Report category boundaries when continuous variables were categorized	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 13, paragraphs 1, 2 and 3
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 3, Strengths and limitations of the study section Page 15, 2on paragraph
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 15, 3rd paragraph
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 16, last sentence
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 17, last paragraph

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.